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=> fil reg
FILE 'REGISTRY' ENTERED AT 11:24:46 ON 08 AUG 2002
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STRUCTURE FILE UPDATES:    7 AUG 2002  HIGHEST RN 443093-92-3
DICTIONARY FILE UPDATES:   7 AUG 2002  HIGHEST RN 443093-92-3

TSCA INFORMATION NOW CURRENT THROUGH January 7, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d sta que l36
L21             STR

                                10
                                 S
                                 >
                                 <
N~~G1~~S~~G2~~G1~~N               C
1   2   3   4   5   6           @8


REP G1=(0-1) 8
REP G2=(1-5) S
NODE ATTRIBUTES:
NSPEC   IS RC     AT   1
NSPEC   IS RC     AT   6
CONNECT IS M1  RC AT   1
CONNECT IS M1  RC AT   6
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS   8

STEREO ATTRIBUTES: NONE
L23             , SCR 1993 AND 2022
L24               SCR 2043 OR 2050 OR 2049 OR 2054 OR 2039
L26         1270 SEA FILE=REGISTRY SSS FUL L21 AND L23 NOT L24
L27               STR

N~~S~~G2~~N
1   2   3   4


REP G2=(1-5) S
NODE ATTRIBUTES:
NSPEC   IS RC     AT   1
NSPEC   IS RC     AT   4
CONNECT IS M1  RC AT   1
CONNECT IS M1  RC AT   4
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 – 703-308-4498
jan.delaval@uspto.gov

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RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS   4

STEREO ATTRIBUTES: NONE
L29          513 SEA FILE=REGISTRY SUB=L26 CSS FUL L27
L30              STR
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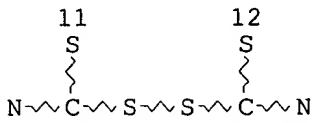


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NODE ATTRIBUTES:
NSPEC    IS RC     AT   1
NSPEC    IS RC     AT   6
CONNECT  IS M1  RC AT   1
CONNECT  IS M1  RC AT   6
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS   8

STEREO ATTRIBUTES: NONE
L32          635 SEA FILE=REGISTRY SUB=L26 CSS FUL L30
L36         1148 SEA FILE=REGISTRY ABB=ON  PLU=ON  (L29 OR L32)

=> d his

     (FILE 'HOME' ENTERED AT 10:04:46 ON 08 AUG 2002)
                SET COST OFF

     FILE 'HCAPLUS' ENTERED AT 10:04:55 ON 08 AUG 2002
                E WO99-AU724/AP,PRN
L1             1 S E3,E4
                E BERNARD H/AU
L2           118 S E3,E10,E15-E17
                E TAN Y/AU
L3            91 S E3,E10
                E TAN YEE/AU
L4            14 S E4
                E BEERHEIDE W/AU
L5             8 S E3,E4
                E TING A/AU
L6            86 S E3,E5
L7            20 S E26,E27
                E SIM M/AU
L8             9 S E3,E10
L9            19 S E31
                E PAPILLOMAVIRUS/CT
                E E3+ALL
L10         5802 S E6,E5+NT
L11        14774 S E4+NT
L12         9994 S ?PAPILLOM?
L13         5007 S HPV? OR MPV?
L14           50 S L2-L9 AND L10-L13
L15            1 S L1 AND L14
L16           49 S L14 NOT L15
L17            2 S L16 AND ?DISULF?
L18            3 S L15,L17
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                SEL RN

     FILE 'REGISTRY' ENTERED AT 10:13:43 ON 08 AUG 2002
L19          105 S E1-E105
L20           80 S L19 AND (N AND S)/ELS
L21              STR
L22            1 S L21 CSS
L23              SCR 1993 AND 2022
L24              SCR 2043 OR 2050 OR 2049 OR 2054 OR 2039
L25            7 S L21 AND L23 NOT L24
L26         1270 S L21 AND L23 NOT L24 FUL
                 SAV L26 KWON763/A
L27              STR L21
L28           28 S L27 CSS SAM SUB=L26
L29          513 S L27 CSS FUL SUB=L26
                 SAV L29 KWON763A/A
L30              STR L21
L31           28 S L30 CSS SAM SUB=L26
L32          635 S L30 CSS FUL SUB=L26
                 SAV L32 KWON763B/A
L33           49 S L20 AND L29,L32
L34           31 S L20 NOT L33
L35              STR L21
L36         1148 S L29,L32
L37           39 S L35 CSS SAM SUB=L36
L38              STR L35
L39           48 S L38 CSS SAM SUB=L36
L40            9 S L39 NOT L37
L41         1007 S L38 CSS FUL SUB=L36
L42          141 S L36 NOT L41

     FILE 'HCAPLUS' ENTERED AT 11:18:48 ON 08 AUG 2002
L43         8760 S L41
L44           98 S L42
L45         2830 S L33
L46         8834 S L43-L45
L47            3 S L2-L9 AND L46
L48           12 S L10-L13 AND L46
L49           12 S L47,L48
                 SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 11:24:02 ON 08 AUG 2002
L50           50 S E106-E155

     FILE 'REGISTRY' ENTERED AT 11:24:46 ON 08 AUG 2002

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 11:25:07 ON 08 AUG 2002
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FILE COVERS 1907 - 8 Aug 2002 VOL 137 ISS 6
FILE LAST UPDATED: 7 Aug 2002 (20020807/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> d l49 all tot

L49 ANSWER 1 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 2002:157589 HCAPLUS
DN 136:210549
TI Retinol binding protein receptor-related treatment of hyperproliferative diseases
IN Ward, Simon; Bavik, Claes; Cork, Michael; Tazi-Ahnini, Rachid
PA University of Sheffield, UK
SO PCT Int. Appl., 139 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-00
CC 1-6 (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002015920	A2	20020228	WO 2001-GB3694	20010817
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2001078632	A5	20020304	AU 2001-78632	20010817
PRAI	GB 2000-20351	A	20000817		
	WO 2001-GB3694	W	20010817		

AB Methods and compns. are provided for treating a patient suffering from a hyperproliferative disorder or photoageing. The methods involve blocking the activity of a retinol binding protein receptor (RBPr) in cells of the patient, and/or administering to the patient an antagonist of a retinol binding protein receptor (RBPr) and/or lowering the endogenous level of retinoic acid (RA) in cells of said patient.

ST retinol binding protein receptor hyperproliferative disease photoaging treatment; retinoic acid redn hyperproliferative disease photoaging treatment

IT Keratins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(1; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Skin, disease
(Darriers disease; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(PPAR response element; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Genetic element

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(RARE (retinoic acid-responsive element); retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(RBP (retinol binding protein); retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Genetic element
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(TRE (thyroid hormone-responsive element); retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Keratosis
(actinic; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Mental disorder
(affective, seasonal; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Antiarteriosclerotics
(antiatherosclerotics; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Bone, disease
(bone growth disorder; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Kidney, neoplasm
(carcinoma, inhibitors; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Lupus erythematosus
(cutaneous; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Angiogenesis
Fertility
Spermatogenesis
(disorder; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Skin, disease
(epidermal naevoid syndromes; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Skin
(epidermis, enhanced or compromised epidermal barrier function; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Keratosis
(epidermolytic hyperkeratosis; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Skin, disease
(erythrokeratodermia variabilis; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Bone, disease
(fracture; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Toxicity
(hepatotoxicity; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Keratosis
(hyper-, palmoplantar; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Keratosis
(hyperkeratosis; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Skin, disease
(hypertrophic scar; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Skin, disease

(ichthyosis; retinol binding protein receptor-related treatment of hyperproliferative diseases)
IT Egg
(implantation, disorder; retinol binding protein receptor-related treatment of hyperproliferative diseases)
IT Cell differentiation
(inducers; retinol binding protein receptor-related treatment of hyperproliferative diseases)
IT Skin, disease
(irritation; retinol binding protein receptor-related treatment of hyperproliferative diseases)
IT Skin
(keratinization, disorder; retinol binding protein receptor-related treatment of hyperproliferative diseases)
IT Skin
(keratinocyte; retinol binding protein receptor-related treatment of hyperproliferative diseases)
IT Antitumor agents
(kidney carcinoma; retinol binding protein receptor-related treatment of hyperproliferative diseases)
IT Skin, disease
(lichen planus; retinol binding protein receptor-related treatment of hyperproliferative diseases)
IT Melanins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(melanogenesis disorder; retinol binding protein receptor-related treatment of hyperproliferative diseases)
IT Antibodies
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monoclonal; retinol binding protein receptor-related treatment of hyperproliferative diseases)
IT Skin, disease
(non-bullous ichthyosiform erythroderma; retinol binding protein receptor-related treatment of hyperproliferative diseases)
IT Skin, disease
(photoaging; retinol binding protein receptor-related treatment of hyperproliferative diseases)
IT Skin, disease
(pigmentation, disorder; retinol binding protein receptor-related treatment of hyperproliferative diseases)
IT Skin, disease
(pityriasis rubra pilaris; retinol binding protein receptor-related treatment of hyperproliferative diseases)
IT Surgery
(post-operative scarring; retinol binding protein receptor-related treatment of hyperproliferative diseases)
IT Alopecia
Antidepressants
Antitumor agents
Antiviral agents
Cirrhosis
Cytotoxic agents
Drug screening
Fibroblast
Hepatitis
Hepatitis C virus
Human herpesvirus
Human immunodeficiency virus
Human papillomavirus
Hypolipemic agents
Keloid

Psoriasis
Wart
Wound healing promoters
(retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Antisense DNA
Antisense RNA
Antisense oligonucleotides
Immunoglobulins
Peptides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(retinol-binding; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Skin, disease
(rosacea; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Antitumor agents
(squamous cell carcinoma; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Osteoporosis
(therapeutic agents; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Liver
(toxicity; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Biological transport
(uptake; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Genetic element
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(vitamin D-responsive element; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Acne
(vulgaris; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT 9031-72-5, Alcohol dehydrogenase 9033-53-8, Retinol dehydrogenase 37250-99-0, Retinal dehydrogenase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(isoforms; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT 68-26-8, Retinol 116-31-4, Retinal 302-79-4, Retinoic acid
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT 401572-74-5
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT 401572-75-6 401572-76-7
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT **97-77-8**, Disulfiram 637-03-6, Phenylarsine oxide 5392-40-5, 3,7-Dimethyl-2,6-octadienal 5697-56-3, Carbenoxolone 7554-65-6, 4-Methylpyrazole
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(retinol binding protein receptor-related treatment of hyperproliferative diseases)
IT 401890-74-2 401890-75-3
RL: PRP (Properties)
(unclaimed nucleotide sequence; retinol binding protein receptor-related treatment of hyperproliferative diseases)

L49 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:906113 HCAPLUS
DN 136:25138
TI Skin patch for use in contact immunotherapy
IN Hopp, Robert B.
PA USA
SO U.S. Pat. Appl. Publ., 15 pp., Cont.-in-part of U.S. Ser. No. 95,700, abandoned.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K039-35
ICS A61K009-70
NCL 424449000
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2001051182	A1	20011213	US 2001-768156	20010125
PRAI US 1996-717108	A2	19960920		
US 1998-95700	B2	19980608		

AB A device, preferably in the form of a skin patch, is disclosed for usage in the delivery of a contactant to human skin for the purpose of treating medical conditions responsive to contact immunotherapy, without the presence of medication to alleviate contact dermatitis induced by the contactant. The skin patch specifically induces a cell-mediated contact dermatitis in the treatment of skin disorders. Its anticipated use pertains to treatment of, for example, human **papilloma** virus infections, or warts. In a first embodiment, a pressure activated single chambered skin patch is topically applied and used for controlled release of contactant to human skin. In a second embodiment, a pressure activated two-chambered skin patch is topically applied and used for controlled release of a contactant to human skin. Alternatively, a single chambered skin patch is topically applied and hydrated by the contacted skin for release of contactant. In an addnl. embodiment, the contactant may be applied sep. of the skin patch portion, in a manner that maintains the contactant in contact with the patient's skin for the predetd. period of time necessary to cause sufficient contact dermatitis to effect resoln. of the medical condition. A single reservoir system for the delivery of squaric acid di-Bu ester to the skin was constructed.
ST skin patch contact immunotherapy
IT Balsams
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Peru; skin patch for use in contact immunotherapy)
IT Alopecia
(areata; skin patch for use in contact immunotherapy)
IT Synthetic rubber, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(black; skin patch for use in contact immunotherapy)

IT Dermatitis
(contact; skin patch for use in contact immunotherapy)
IT Lymphocyte
(induction; skin patch for use in contact immunotherapy)
IT AIDS (disease)
Immunotherapy
Papillomavirus
Perfumes
Vitiligo
(skin patch for use in contact immunotherapy)
IT Epoxy resins, biological studies
Rosin
Thiols (organic), biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(skin patch for use in contact immunotherapy)
IT Drug delivery systems
(topical; skin patch for use in contact immunotherapy)
IT Drug delivery systems
(transdermal; skin patch for use in contact immunotherapy)
IT Alcohols, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(wool; skin patch for use in contact immunotherapy)
IT 50-00-0, Formaldehyde, biological studies 54-64-8, Thimerosal 91-22-5, Quinoline, biological studies 98-54-4, p-tert-Butylphenol 99-96-7D, p-Hydroxybenzoic acid, esters 106-50-3, p-Phenylenediamine, biological studies **137-26-8**, Thiuram 149-30-4, Mercaptobenzothiazole 333-18-6, Ethylenediamine dihydrochloride 886-38-4, Diphenylcyclopropenone 1405-10-3, Neomycin sulfate 2892-62-8, Squaric acid dibutyl ester 4080-31-3, Quaternium 15 7646-79-9, Cobalt dichloride, biological studies 7778-50-9, Potassium dichromate 7786-81-4, Nickel sulfate 25567-67-3, Dinitrochlorobenzene 26172-55-4
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(skin patch for use in contact immunotherapy)

L49 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:840664 HCAPLUS
DN 134:110110
TI Inactivation of the human **papillomavirus**-16 E6 oncoprotein by organic disulfides
AU **Beerheide, Walter; Sim, Mui Mui; Tan, Yee-Joo ; Bernard, Hans-Ulrich; Ting, Anthony E.**
CS Drug Screen Development Laboratory, Institute of Molecular and Cell Biology, Singapore, 117609, Singapore
SO Bioorganic & Medicinal Chemistry (2000), 8(11), 2549-2560
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Science Ltd.
DT Journal
LA English
CC 1-3 (Pharmacology)
Section cross-reference(s): 21
AB We are investigating compds. that could be useful in the treatment of neoplastic lesions of the cervix by acting on the oncoprotein E6 of human **papillomavirus**-16. The E6 protein contains two potential zinc-binding domains that are required for most of its functions. We have published tests that measure (i) the release of zinc ions after chem. alteration of the cysteine groups of these zinc-binding domains (TSQ assay), (ii) the interaction of E6 with the cellular proteins E6AP and E6BP (BIACORE assay), and (iii) the viability of tumor cell lines that require the continuous expression of **HPV** oncoproteins (WST1 assay). Based on these tests, we identified 4,4'-dithiodimorpholine as a

potential lead compd. In this study we examd. whether the dithiobisamine moiety of 4,4'-dithiodimorpholine may be an important mol. prerequisite for further drug development in this system. We have evaluated 59 new substances including org. disulfides and those contg. the dithiobisamine moiety, as well as structural analogs. The compds. with significant reactivity in all three assays were obsd. only for dithiobisamine derivs. with satd. cyclic amines and aryl substituted piperazines. The identity of these substances suggests that the N-S-S-N moiety is necessary but not sufficient for reactivity in our assays, and that dithiobisamine based substances are useful as lead compds. that target the cysteine groups of **HPV**-16 E6 zinc fingers.

ST disulfide org prepn **papillomavirus** oncoprotein inactivation; cervix neoplasm inhibitor org disulfide prepn

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(E6; prepn. of org. disulfides and inactivation of human **papillomavirus**-16 E6 oncoprotein)

IT Uterus, neoplasm
(cervix, inhibitors; prepn. of org. disulfides and inactivation of human **papillomavirus**-16 E6 oncoprotein)

IT Antitumor agents
(cervix; prepn. of org. disulfides and inactivation of human **papillomavirus**-16 E6 oncoprotein)

IT **Human papillomavirus 16**
Structure-activity relationship
(prepn. of org. disulfides and inactivation of human **papillomavirus**-16 E6 oncoprotein)

IT Amines, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(secondary; prepn. of org. disulfides and inactivation of human **papillomavirus**-16 E6 oncoprotein)

IT Protein motifs
(zinc-binding domain; prepn. of org. disulfides and inactivation of human **papillomavirus**-16 E6 oncoprotein)

IT **729-46-4P** 1013-93-0P 1468-28-6P **2129-27-3P**
5328-68-7P **6542-61-6P 7764-30-9P 10220-20-9P**
15575-30-1P 16131-50-3P 17376-42-0P 36903-85-2P
36938-10-0P 59226-72-1P 62158-06-9P
72896-38-9P 85865-96-9P 98999-00-9P
103388-17-6P 260973-66-8P 260973-72-6P
260973-79-3P 260973-81-7P 260973-83-9P
260973-85-1P 303796-55-6P 320609-04-9P
320609-05-0P 320609-06-1P 320609-07-2P
320609-08-3P 320609-09-4P 320609-10-7P
320609-11-8P 320609-12-9P 320609-13-0P
320609-14-1P 320609-15-2P 320609-16-3P
320609-17-4P 320609-18-5P 320609-19-6P
320609-21-0P 320609-22-1P 320609-23-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of org. disulfides and inactivation of human **papillomavirus**-16 E6 oncoprotein)

IT **103-34-4** 120-78-5 880-09-1 **1623-84-3**
1623-85-4 2127-10-8 2550-40-5 3256-06-2,
Thioperoxydicarbonimidic diamide ([(H2N)C(NH)]2S2) 5117-07-7
14193-38-5 15658-35-2 **26087-98-9** 61747-35-1 66304-01-6
66546-28-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of org. disulfides and inactivation of human

papillomavirus-16 E6 oncoprotein)
IT 85-46-1, Naphthalene-1-sulfonyl chloride 98-88-4, Benzoyl chloride
110-91-8, Morpholine, reactions 1122-82-3, Cyclohexyl isothiocyanate
6160-65-2, 1,1'-Thiocarbonyl diimidazole 7693-46-1, 4-Nitrophenyl
chloroformate 10025-67-9, Disulfur dichloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of org. disulfides and inactivation of human
papillomavirus-16 E6 oncoprotein)
RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Barbosa, M; Oncogene 1989, V4, P1529 HCAPLUS
(2) Beerheide, W; J Natl Cancer Inst 1999, V91, P1211 HCAPLUS
(3) Borch, R; Proc Natl Acad Sci 1979, V76, P6611 HCAPLUS
(4) Butz, K; Oncogene 1995, V10, P927 HCAPLUS
(5) Chan, S; J Virol 1995, V69, P3074 HCAPLUS
(6) Chen, J; Science 1995, V269, P529 HCAPLUS
(7) Crook, T; Cell 1991, V67, P547 HCAPLUS
(8) Diaz, C; Phosphorus, Sulfur, and Silicon 1989, V44, P1
(9) Dyson, N; Science 1989, V243, P934 HCAPLUS
(10) Frank, N; Toxicology 1995, V95, P113 HCAPLUS
(11) Fritsche, M; Oncogene 1993, V8, P307 HCAPLUS
(12) Gao, Q; Mol Cell Biol 1999, V19, P733 HCAPLUS
(13) Gross-Mesilaty, S; Proc Natl Acad Sci 1998, V95, P8058 HCAPLUS
(14) Grossman, S; Oncogene 1989, V4, P1089 HCAPLUS
(15) Hathout, Y; Drug Metab Dispos 1996, V24, P1395 HCAPLUS
(16) Huibregtse, J; Mol Cell Biol 1993, V13, P775 HCAPLUS
(17) International Agency for Research on Cancer; IARC Monographs on the evaluation of carcinogenic risks to humans 1995, V64
(18) Katritzky, A; SYNLETT 1990, V8, P473
(19) Keys, H; N Engl J Med 1999, V340, P1154 HCAPLUS
(20) Kovacich, J; J Thorac Cardiovasc Surg 1999, V118, P154 HCAPLUS
(21) Kukimoto, I; Biochem Biophys Res Commun 1998, V249, P258 HCAPLUS
(22) Lamberti, C; EMBO J 1990, V9, P1907 HCAPLUS
(23) Liu, G; Mol Carcinog 1998, V22, P235 HCAPLUS
(24) Liu, Y; J Virol 1999, V73, P7297 HCAPLUS
(25) Malmqvist, M; Curr Opin Immunol 1993, V5, P282 HCAPLUS
(26) Morris, M; N Engl J Med 1999, V340, P1137 MEDLINE
(27) Myers, G; Human Papillomaviruses 1995, P47
(28) Osswald, H; J Cancer Res Clin Oncol 1990, V116, P448 MEDLINE
(29) Perchellet, J; Cancer Res 1987, V47, P6302 HCAPLUS
(30) Rapp, L; Biochim Biophys Acta 1998, V1378, P1
(31) Reisinger, E; Lancet 1990, V335, P679 MEDLINE
(32) Rice, W; J Med Chem 1996, V39, P3606 HCAPLUS
(33) Rice, W; Science 1995, V270, P1194 HCAPLUS
(34) Ronco, L; Genes Dev 1998, V12, P2061 HCAPLUS
(35) Rose, P; N Engl J Med 1999, V340, P1144 HCAPLUS
(36) Rothenberg, M; J Natl Cancer Inst 1988, V80, P1488 MEDLINE
(37) Scheffner, M; Proc Natl Acad Sci 1994, V91, P8797 HCAPLUS
(38) Siegers, C; Arch Toxicol 1978, V41, P79 HCAPLUS
(39) Song, S; J Virol 1999, V73, P5887 HCAPLUS
(40) Stoler, M; Hum Pathol 1992, V23, P117 MEDLINE
(41) Tan, T; Cancer Res 1995, V55, P4599 HCAPLUS
(42) Thomas, M; Oncogene 1998, V17, P2943 HCAPLUS
(43) Tong, X; Proc Natl Acad Sci 1997, V94, P4412 HCAPLUS
(44) Tummino, P; Proc Natl Acad Sci 1996, V93, P969 HCAPLUS
(45) Ullman, C; Biochem J 1996, V319, P229 HCAPLUS
(46) von Knebel, D; Int J Cancer 1992, V51, P831
(47) White, A; Genes Dev 1994, V8, P666 HCAPLUS
(48) Zimmermann, H; J Virol 1999, V73, P6209 HCAPLUS
(49) zur Hausen, H; Annu Rev Microbiol 1994, V48, P427 MEDLINE

L49 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:456859 HCAPLUS

DN 133:79356
TI Synthetic and therapeutic methods for the alpha and beta domains of metallothionein
IN Vallee, Bert L.
PA USA
SO PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K009-14
ICS A61K009-70; A61K038-17; C07K001-04; C07K001-06; C07K001-16; C07K014-825
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 2, 4, 8, 34
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000038654	A1	20000706	WO 1999-US30573	19991221

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1998-113459P P 19981223
AB The present invention relates to the alpha and beta domains of metallothionein and analogs thereof, their synthesis, and therapeutic applications of them. Purified metal-free and metal-contg. alpha and beta domains of metallothionein are provided. A high yield method of synthesis and purifn. is also provided for the metal-free and metal-contg. alpha and beta domains of metallothionein. Finally, therapeutic methods are provided that use the alpha and beta domains of metallothionein to transport selected metals to specific tissues or to sequester metals from these tissues in order to treat conditions in those tissues that are ameliorated by the addn. or sequestration of these metals.
ST metallothionein domain metal sequestration tissue targeting
IT Hepatitis
(C; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Protective groups
(CBZ; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Intestine, disease
(Crohn's; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Protective groups
(Fmoc; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Imaging
(NMR, reagents for; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Appetite
(anorexia nervosa; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Antigens
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(antibodies specific for; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Prostate gland

(benign hyperplasia; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Appetite
(bulimia; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT **Papillomavirus**
(carcinogenesis; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Heart, disease
(cardiomyopathy; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Drug delivery systems
(carriers; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Nervous system
(central, disease; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Intestine, disease
(colitis; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Dialysis
(complications from kidney-related; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Threads
Threads
(cotton, supports; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Disease, animal
(deficiency, for metals; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Nervous system
(degeneration; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Digestive tract
Endocrine system
Parathyroid gland
Skeleton
(disease; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Circulation
Immunity
Vision
(disorder; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Radiation
(exposure, disease from; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Proteins, specific or class
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(immobilized; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Human immunodeficiency virus
(infection; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Drug delivery systems
(injections, i.v.; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Chemotherapy
(injury from; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Infection
(measles; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Antibodies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metallothionein domains bound to; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Prostate gland
Prostate gland
(neoplasm, inhibitors; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Nerve, disease
(neuropathy; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Keratosis
(parakeratosis; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Apoptosis
(pathol.; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Actinides
Main group elements
Rare earth metals, biological studies
Transition metals, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(peptide domains contg.; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Solid phase synthesis
(peptide; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Blood vessel, disease
(peripheral; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Antitumor agents
(prostate gland; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Eye, disease
(retinitis pigmentosa; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Metals, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(sequestration of; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Chromatography
Paper
(supports; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Fibers
Glass beads
RL: NUU (Other use, unclassified); USES (Uses)
(supports; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Drug delivery systems
(suppositories; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Peptides, preparation
RL: PNU (Preparation, unclassified); PREP (Preparation)
(synthesis of; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT AIDS (disease)
Adrenal gland, disease
Alcoholism
Alopecia

Alzheimer's disease
Anti-AIDS agents
Anti-Alzheimer's agents
Anti-inflammatory agents
Antiarthritics
Anticonvulsants
Antidiarrheals
Antiobesity agents
Antiparkinsonian agents
Antitumor agents
Antiviral agents
Asthma
Binders
Buffers
Common cold
Drug delivery systems
Drug dependence
Drug targeting
Emulsifying agents
Epilepsy
Fluorescent substances
Gel permeation chromatography
Hemochromatosis
Infection
Mental disorder
Neoplasm
Obesity
Osteoarthritis
Ovary, disease
Parkinson's disease
Particle size distribution
Preparative chromatography
Protein motifs
Protein sequences
Semliki Forest virus
Sequestering agents
Skin, disease
Thyroid gland, disease
Transformation, neoplastic
Wetting agents
Wilson's disease
(synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Metallothioneins
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Radionuclides, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Lupus erythematosus
(systemic; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Protective groups
(t-Boc; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Cotton fibers
Cotton fibers
(threads, supports; synthetic and therapeutic methods for the alpha and

beta domains of metallothionein)
IT Muscle, disease
(white muscle disease of lambs; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT Sheep
(white muscle disease of; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT 100-68-5, Thioanisole 108-95-2, Phenol, uses 7732-18-5, Water, uses 7761-88-8, Silver(I) nitrate, uses 26914-40-9, Ethanedithiol
RL: NUU (Other use, unclassified); USES (Uses)
(cleaving soln. contg.; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT 106-89-8, Epichlorohydrin, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(dextran crosslinker; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT 9004-54-0, Dextran, analysis
RL: ARU (Analytical role, unclassified); DEV (Device component use); PEP (Physical, engineering or chemical process); ANST (Analytical study); PROC (Process); USES (Uses)
(gel filtration chromatog. with; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT 7429-90-5, Aluminum, biological studies 7439-89-6, Iron, biological studies 7439-91-0, Lanthanum, biological studies 7439-96-5, Manganese, biological studies 7439-98-7, Molybdenum, biological studies 7440-02-0, Nickel, biological studies 7440-22-4, Silver, biological studies 7440-24-6, Strontium, biological studies 7440-26-8, Technetium, biological studies 7440-33-7, Tungsten, biological studies 7440-38-2, Arsenic, biological studies 7440-39-3, Barium, biological studies 7440-43-9, Cadmium, biological studies 7440-50-8, Copper, biological studies 7440-57-5, Gold, biological studies 7440-58-6, Hafnium, biological studies 7440-66-6, Zinc, biological studies 7440-69-9, Bismuth, biological studies 7440-70-2, Calcium, biological studies 7782-49-2, Selenium, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(peptide domains contg.; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT 9003-53-6D, Polystyrene, functionalized derivs.
RL: NUU (Other use, unclassified); USES (Uses)
(supports; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT 56-65-5, 5'-Atp, biological studies 70-18-8, Glutathione, biological studies 86-01-1, 5'-Gtp **97-77-8**, Disulfiram
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT 7440-48-4, Cobalt, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
IT 76-05-1, Trifluoroacetic acid, uses
RL: NUU (Other use, unclassified); USES (Uses)
(synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Bofill; Journal of Inorganic Biochemistry 1999, V73, P57 HCAPLUS
(2) Goldenberg; US 5736119 A 1998 HCAPLUS
(3) Kull; Journal of the American Chemical Society 1990, V112(6), P2291 HCAPLUS

(4) Nielson; The Journal Of Biological Chemistry 1985, V260(15), P8698 HCAPLUS
(5) Pan; Biochemical And Biophysical Research Communications 1994, V202(1), P621 HCAPLUS
(6) Riniker; US 3910872 A 1975 HCAPLUS
(7) Tolman, G; US 4732864 A 1988 HCAPLUS
(8) Winge; The Journal Of Biological Chemistry 1984, V259, P11419 HCAPLUS
(9) Yoshida; Proceedings of the National Academy of Science USA 1979, V76(1), P486 HCAPLUS

L49 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:175791 HCAPLUS
DN 132:222549
TI Preparation of bis(piperazinyl) disulfides and analogs for treatment of **papillomavirus**-mediated disorders
IN **Bernard, Hans-Ulrich; Tan, Yee Joo; Beerheide, Walter; Ting, Anthony Eugene; Sim, Mui Mui**
PA Institute of Molecular & Cell Biology, Singapore; Hughes, E. John L.
SO PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D203-24
ICS C07D205-04; C07D207-48; C07D209-48; C07D211-96; C07D213-76; C07D239-28; C07D239-42; C07D243-08; C07D263-04; C07D265-30; C07D295-194; C07D295-26; C07D317-58; C07C323-49; C07C333-32; C07C381-00; A61K031-13; A61K031-145; A61K031-535
CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000014063	A1	20000316	WO 1999-AU724	19990903
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9958401	A1	20000327	AU 1999-58401	19990903
	EP 1112250	A1	20010704	EP 1999-945758	19990903
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002524442	T2	20020806	JP 2000-568822	19990903
PRAI	AU 1998-5733	A	19980904		
	AU 1999-1645	A	19990715		
	WO 1999-AU724	W	19990903		

OS MARPAT 132:222549
AB R1R2NZSSnZNR3R4 (I) [R1-R4 = H, alkyl, acyl, aryl, etc.; R1R2,R3R4 = (CH2)lUm(CH2)p; U = bond, O, S, NH, CH2; Z = bond or where n = 1 Z may = CS; l,p = 0-6; m = 0 or 1; l+m+p.gtoreq.2; n = 1-5], inhibitors of proteins encoded by an **MPV** gene by disruption of a chelated metal cation domain, were prepd. Thus, e.g., R1R2NSSNR3R4 (R1R2,R3R4 = CH2CH2NRCH2CH2, R = 2-pyridinyl) was prepd. Data for biol. activity of I were given.
ST piperazinyl disulfide prepn treatment **papillomavirus** mediated disorder
IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(E6; prepn. of bis(piperazinyl) disulfides and analogs for treatment of

papillomavirus-mediated disorders)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(E7; prepn. of bis(piperazinyl) disulfides and analogs for treatment of **papillomavirus**-mediated disorders)

IT Uterus, neoplasm
Uterus, neoplasm
(cervix, inhibitors; prepn. of bis(piperazinyl) disulfides and analogs for treatment of **papillomavirus**-mediated disorders)

IT Antitumor agents
(cervix; prepn. of bis(piperazinyl) disulfides and analogs for treatment of **papillomavirus**-mediated disorders)

IT Transforming proteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibitors; prepn. of bis(piperazinyl) disulfides and analogs for treatment of **papillomavirus**-mediated disorders)

IT **Human papillomavirus 16**
Human papillomavirus 18
Papillomavirus
(prepn. of bis(piperazinyl) disulfides and analogs for treatment of **papillomavirus**-mediated disorders)

IT **103-34-4P 729-46-4P 1623-84-3P**
1623-85-4P 2759-28-6DP, N-Benzylpiperazine, 4,4'-polythiobis deriv. **6542-61-6P 7764-30-9P 10220-20-9P**
15575-30-1P 26087-98-9P 35386-24-4DP, 1-(2-Methoxyphenyl)piperazine, 4,4'-polythiobis deriv. **36938-10-0P**
59226-72-1P 85865-96-9P 98999-00-9P
260973-66-8P 260973-68-0P 260973-72-6P
260973-74-8P 260973-75-9P 260973-76-0P
260973-79-3P 260973-81-7P 260973-83-9P
260973-85-1P 260973-87-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of bis(piperazinyl) disulfides and analogs for treatment of **papillomavirus**-mediated disorders)

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Anon
(2) Anon; Chromatographia 1989, 3-4, P113 HCAPLUS
(3) Anon; Rubber Chem Technol 1984, 4, P744 HCAPLUS
(4) Bridgestone Corporation; EP 562750 1993 HCAPLUS
(5) Chertova, E; Techniques in Protein Chemistry VIII [Symp Protein Soc], 10th 1997, P231 HCAPLUS
(6) Hathout, Y; Drug Metabolism and Disposition:The Biological Fate of Chemicals 1996, V24(12), P1395 HCAPLUS
(7) Katritzky, A; Synlett 1990, P473 HCAPLUS
(8) Kawaguchi Kagaku Kogyo Kk; JP 04208223 1992 HCAPLUS
(9) Kinki Daigaku Gh; JP 07233057 A 1995 HCAPLUS
(10) Kuraray Kk; JP 03063258 A 1991 HCAPLUS
(11) Lycke, E; Brain Research 1972, V44(2), P603 MEDLINE
(12) McDonnell, N; Journal of Medicinal Chemistry 1997, V40(13), P1969 HCAPLUS
(13) Nihon Parkerizing; JP 02304346 A 1990 HCAPLUS
(14) Nippon Oil Seal Ind; JP 03178148 A 1988
(15) Ott, D; Virology 1998, V243, P287
(16) Rein, A; Journal of Virology 1990, V70(8), P4966
(17) Rice, W; Journal of Medicinal Chemistry 1996, V39(19), P3606 HCAPLUS
(18) Rotstein, J; Carcinogenesis 1988, V9(9), P1547 HCAPLUS
(19) The Government Of The United States Of America; WO 9609406 1996 HCAPLUS
(20) Toyo Soda Mfg Kk; JP 1207376 A 1986

L49 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:507293 HCAPLUS
DN 132:87659
TI Potential drugs against cervical cancer: zinc-ejecting inhibitors of the human **papillomavirus** type 16 E6 oncoprotein
AU **Beerheide, Walter; Bernard, Hans-Ulrich; Tan, Yee-Joo**; Ganesan, Arasu; Rice, William G.; **Ting, Anthony E.**
CS Screening for Novel Inhibitors Laboratory, Institute of Molecular and Cell Biology, Singapore, 117609, Singapore
SO Journal of the National Cancer Institute (1999), 91(14), 1211-1220
CODEN: JNCIEQ; ISSN: 0027-8874
PB Oxford University Press
DT Journal
LA English
CC 1-1 (Pharmacology)
Section cross-reference(s): 10
AB The principal agent in the etiol. of cervical cancer, i.e., human **papillomavirus** (**HPV**) type 16, encodes three oncoproteins, E5, E6, and E7. Structural and mutational studies have identified two potential zinc-finger domains as crit. for E6 protein function. We investigated several assays to identify and characterize compds. that interfere with the binding of zinc to E6. Thirty-six compds. were selected on the basis of their structure, which would facilitate their participation in sulfhydryl residue-specific redox reactions, and were tested for their ability to release zinc from E6 protein. The zinc-ejecting compds. were then tested for their ability to inhibit E6 binding to E6-assocd. protein (E6AP) and E6-binding protein (E6BP), two coactivators of E6-mediated cellular transformation. The binding of E6 to E6BP and E6AP was measured by use of surface plasmon resonance (a technique that monitors mol. interactions by measuring changes in refractive index) and by use of in vitro translation assays. The compds. were also tested for their effects on the viability of **HPV** -contg. cell lines. Nine of the 36 tested compds. ejected zinc from E6. Two of the nine compds. inhibited the interaction of E6 with E6AP and E6BP, and one of these two, 4,4'-dithiodimorpholine, selectively inhibited cell viability and induced higher levels of p53 protein (assocd. with the induction of apoptosis [programmed cell death]) in tumorigenic **HPV** -contg. cells. We have described assay systems to identify compds., such as 4,4'-dithiodimorpholine, that can potentially interfere with the biol. and pathol. of **HPV**. These assay systems may be useful in the development of drugs against cervical cancer, genital warts, and asymptomatic infections by genital **HPVs**.
ST assay **HPV** cervical cancer inhibitor design; human **papillomavirus** cervical cancer inhibitor assay; zinc binding oncoprotein **HPV** antitumor assay; redox reaction antiviral **HPV** design assay; p53 apoptosis cervical cancer inhibitor assay
IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(E5; potential drugs against cervical cancer)
IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(E6; potential drugs against cervical cancer)
IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(E7; potential drugs against cervical cancer)
IT Antiviral agents
(anti- **HPV**; potential drugs against cervical cancer)
IT Uterus, neoplasm
Uterus, neoplasm
(cervix, inhibitors; potential drugs against cervical cancer)

IT Antitumor agents
(cervix; potential drugs against cervical cancer)
IT Analysis
Apoptosis
Drug design
Drug screening
Human papillomavirus
Redox reaction
(potential drugs against cervical cancer)
IT p53 (protein)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(potential drugs against cervical cancer)
IT Fusion proteins (chimeric proteins)
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(potential drugs against cervical cancer)
IT 56-17-7, Cystamine dihydrochloride 56-89-3, Cystine, analysis 69-78-3 **97-77-8**, Tetraethylthiuram disulfide 100-32-3 103-33-3, Azobenzene **103-34-4** 119-80-2 120-78-5, 2,2'-Dithiobis(benzothiazole) 123-77-3, Azodicarbonamide 135-57-9, Bis(2-benzamidophenyl)disulfide 150-60-7, Dibenzyl disulfide 537-91-7, Bis(3-Nitrophenyl)disulfide 586-96-9, Nitrosobenzene 644-32-6, Benzoyl disulfide 870-93-9, DL-Homocystine 882-33-7, Phenyl disulfide 940-69-2, .alpha.-Lipoamide 1141-88-4, 2,2'-Dithiodianiline 1155-00-6, Bis(2-nitrophenyl)disulfide 1160-68-5 2127-03-9, Aldrithiol 2 5398-51-6 13895-38-0, 4-Nitrosoresorcinol-1-monomethyl ether 15441-06-2, 3,3'-Dithiodipropionic acid dimethyl ester 16766-09-9, Bis(4-Acetamidophenyl)disulfide 26907-82-4 47231-30-1 108872-98-6 120586-49-4, 1,2-Dithiane-4,5-diol, 1,1-dioxide, cis 207802-09-3
RL: ANT (Analyte); ANST (Analytical study)
(potential drugs against cervical cancer)
IT 7440-66-6, Zinc, biological studies 50812-37-8, Glutathione S-transferase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(potential drugs against cervical cancer)
RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Androphy, E; EMBO J 1987, V6, P989 HCAPLUS
(2) Bartsch, D; EMBO J 1992, V11, P2283 HCAPLUS
(3) Bosch, F; J Virol 1990, V64, P4743 HCAPLUS
(4) Chan, S; J Virol 1995, V69, P3074 HCAPLUS
(5) Chen, J; J Biol Chem 1998, V273, P13537 HCAPLUS
(6) Chen, J; Science 1995, V269, P529 HCAPLUS
(7) Crook, T; Cell 1991, V67, P547 HCAPLUS
(8) Dalal, S; J Virol 1996, V70, P683 HCAPLUS
(9) Daniels, P; FEBS Lett 1997, V416, P6 HCAPLUS
(10) Desaintes, C; EMBO J 1997, V16, P504 HCAPLUS
(11) Dsouza, M; Trends Genet 1997, V13, P497 HCAPLUS
(12) Etscheid, B; Virology 1994, V205, P583 HCAPLUS
(13) Frederickson, C; J Neurosci Methods 1987, V20, P91 HCAPLUS
(14) Grossman, S; Oncogene 1989, V4, P1089 HCAPLUS
(15) Hawley-Nelson, P; EMBO J 1989, V8, P3905 HCAPLUS
(16) Howley, P; Field's virology 1996, P2045
(17) Huibregtse, J; Mol Cell Biol 1993, V13, P775 HCAPLUS
(18) International Agency for Research on Cancer; Human papillomaviruses 1995, V64
(19) Kanda, T; Virology 1991, V185, P536 HCAPLUS
(20) Kearns, P; Drug Discov Today 1998, V3, P113 HCAPLUS
(21) Klingelhutz, A; Nature 1996, V380, P79 HCAPLUS
(22) Klug, A; FASEB J 1995, V9, P597 HCAPLUS
(23) Lamberti, C; EMBO J 1990, V9, P1907 HCAPLUS
(24) Lehman, T; Carcinogenesis 1993, V14, P1491 HCAPLUS

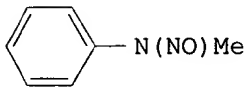
(25) Lehman, T; Carcinogenesis 1993, V14, P833 HCAPLUS
(26) Mackay, J; Trends Biochem Sci 1998, V23, P1 HCAPLUS
(27) Malmqvist, M; Curr Opin Immunol 1993, V5, P282 HCAPLUS
(28) Meyers, G; Human papillomaviruses 1994, PII-E6
(29) Meyers, G; Human papillomaviruses 1995, P47
(30) Nakagawa, S; Virology 1995, V212, P535 HCAPLUS
(31) Polyak, K; Nature 1997, V389, P300 HCAPLUS
(32) Rice, W; J Med Chem 1996, V39, P3606 HCAPLUS
(33) Rice, W; Nat Med 1997, V3, P341 HCAPLUS
(34) Rice, W; Nature 1993, V361, P473 HCAPLUS
(35) Rice, W; Proc Natl Acad Sci 1992, V89, P7703 HCAPLUS
(36) Rice, W; Science 1995, V270, P1194 HCAPLUS
(37) Scheffner, M; Proc Natl Acad Sci 1994, V91, P8797 HCAPLUS
(38) Sedman, S; J Virol 1991, V65, P4860 HCAPLUS
(39) Sherman, L; Virology 1997, V237, P296 HCAPLUS
(40) Stanley, M; Papillomavirus Rep 1994, V5, P141
(41) Steele, C; Cancer Res 1992, V52, P4706 HCAPLUS
(42) Tan, T; Cancer Res 1995, V55, P4599 HCAPLUS
(43) Tew, K; Cancer Res 1994, V54, P4313 HCAPLUS
(44) Tong, X; Proc Natl Acad Sci 1997, V94, P4412 HCAPLUS
(45) Tummino, P; Proc Natl Acad Sci 1996, V93, P969 HCAPLUS
(46) Ullman, C; Biochem J 1996, V319, P229 HCAPLUS
(47) Vandevelde, M; AIDS Res Hum Retroviruses 1996, V12, P567 HCAPLUS
(48) von Knebel Doeberitz, M; Int J Cancer 1992, V51, P831 MEDLINE
(49) Vousden, K; J Virol 1989, V63, P2340 HCAPLUS
(50) White, A; Genes Dev 1994, V8, P666 HCAPLUS
(51) Wright, T; Papillomavirus Rep 1994, V5, P175
(52) Yu, X; Chem Res Toxicol 1995, V8, P586 HCAPLUS
(53) zur Hausen, H; Annu Rev Microbiol 1994, V48, P427 MEDLINE

L49 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 1996:196542 HCAPLUS
DN 124:223463
TI Carcinogenic and cocarcinogenic studies of thiram on mouse skin
AU Shukla, Y.; Baqar, S. M.; Mehrotra, N. K.
CS Industrial Toxicology Res. Centre, Mahatma Gandhi Marg, Lucknow, 226 001, India
SO Food Chem. Toxicol. (1996), 34(3), 283-9
CODEN: FCTOD7; ISSN: 0278-6915
DT Journal
LA English
CC 4-6 (Toxicology)
AB In the present study, the tumorigenic potential of thiram was evaluated in Swiss albino mice by a 2-stage initiation-promotion protocol and a long-term in vivo bioassay for carcinogenicity. Following tumor initiation with thiram and promotion with 12-O-tetradecanoylphorbol 13-acetate, skin tumors developed, mostly at the site of treatment (dorsal skin) in single and multiple dose-initiated animals. Similarly, **papillomatous** growths were obsd. on the dorsal skin of the mice initiated with a single subcarcinogenic dose of dimethylbenzanthracene and promoted with thiram. Thiram failed to provoke tumorigenesis when tested as a complete carcinogen for up to 52 wk and thereafter the study was terminated due to increased mortality. Thus, thiram has both tumor-initiating and tumor-promoting potential in both sexes of Swiss albino mice following topical exposure at the tested dose level.
ST skin tumor promotion thiram
IT Skin, neoplasm
(carcinogenic and cocarcinogenic studies of thiram on skin)
IT Carcinogens
(promoters, carcinogenic and cocarcinogenic studies of thiram on skin)
IT **137-26-8**, Thiram
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(carcinogenic and cocarcinogenic studies of thiram on skin)

L49 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 1988:563075 HCAPLUS
DN 109:163075
TI Effect of exogenous glutathione on tumor progression in the murine skin multistage carcinogenesis model
AU Rotstein, Joel B.; Slaga, Thomas J.
CS Cancer Cent., Univ. Texas Syst., Smithville, TX, 78957, USA
SO Carcinogenesis (London) (1988), 9(9), 1547-51
CODEN: CRNGDP; ISSN: 0143-3334
DT Journal
LA English
CC 1-6 (Pharmacology)
Section cross-reference(s): 4, 14
AB Oxidative stress has been suggested to play an integral role in the cancer process. It may be particularly significant during tumor progression, where there is likely to be a large amt. of free radicals generated by infiltrating inflammatory cells and dying tumor cells. In order to test this hypothesis, a variety of free radical scavengers and antioxidants were assessed for their ability to inhibit tumor progression. The murine skin multistage carcinogenesis model was used to generate **papillomas**, which are a population of putative precancerous lesions. Various test agents were applied topically to **papillomas** in order to det. if they would decrease the incidence of the malignant lesion, squamous cell carcinoma. The agents tested included: GSH, BHA, vitamin E, copper(II) (3,5-diisopropylsalicylate)2, sodium benzoate, N-acetyl cysteine and disulfiram. Under the conditions of the expts., only GSH and disulfiram inhibited tumor progression to a significant degree. Addnl. studies indicated that GSH prevented cancer development in a dose-dependent manner. Another expt. demonstrated that when **papillomas** received repeated topical applications of diethylmaleate, a GSH-depleting agent, tumor progression was enhanced. Collectively these data suggest that sufficient glutathione levels may be important in preventing cancer formation.
ST neoplasm oxidative stress antioxidant; free radical scavenger neoplasm; GSH tumor progress inhibition; disulfiram tumor progress inhibition
IT Neoplasm inhibitors
(antioxidants and free radical scavengers, disulfiram and DSH in relation to)
IT Radicals, biological studies
RL: BIOL (Biological study)
(scavengers, tumor progression inhibition response to)
IT Skin, neoplasm
(treatment of, with antioxidants and free radical scavengers, disulfiram and GSH in relation to)
IT Antioxidants
(tumor progression inhibition response to)
IT 59-02-9, D-.alpha.-Tocopherol 70-18-8, GSH, biological studies
97-77-8, Disulfiram 532-32-1, Sodium benzoate 616-91-1, n-Acetylcysteine 21246-18-4 25013-16-5, BHA
RL: BIOL (Biological study)
(tumor progression inhibition response to)

L49 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 1987:28723 HCAPLUS
DN 106:28723
TI Modifying effects of disulfiram on DNA adduct formation and persistence of benzaldehyde in N-nitroso-N-methylbenzylamine-induced carcinogenesis in rats
AU Schweinsberg, F.; Danecki, S.; Grotzke, J.; Von Karsa, L.; Buerkle, V.
CS Hygiene-Inst., Univ. Tuebingen, Tuebingen, D-7400, Fed. Rep. Ger.
SO J. Cancer Res. Clin. Oncol. (1986), 112(2), 75-80
CODEN: JCROD7; ISSN: 0171-5216

DT Journal
LA English
CC 4-6 (Toxicology)
Section cross-reference(s): 1
GI



I

AB The effects were studied of disulfiram (DSF) [**97-77-8**] on long-term application of N-nitroso-N-methylbenzylamine (NMBA)(I) [937-40-6]. HPLC and fluorescence detection were used to det. O6-methylguanine (O6-MG) [20535-83-5] in DNA obtained from the respiratory tract of rats subjected to long-term simultaneous application of DSF and NMBA. After 2 days of treatment, more O6-MG was detected in the proximal portion of the respiratory tract, including the trachea and main bronchi, than in the distal portion. The findings were reversed after 10 and 30 days, at which time formation of the DNA adduct was substantially higher in the distal portion of the respiratory tract, despite increases in both portions. The biochem. results corresponded to morphol. findings. Initially, increased nos. of metabolizing goblet cells appeared in mucous cell hyperplasia in the proximal respiratory tract. Subsequently, the hyperplasia migrated to distal regions of the respiratory tract; at this stage, the goblet cells disappeared from the proximal portion, which now revealed toxic degeneration, atrophy, and subsequent squamous metaplasia of the mucous lining and squamous **papillomas**. At various times during a 40-day period, 2-7-fold more O6-MG in pulmonary DNA was detected in rats treated with DSF and NMBA than with NMBA alone, whereby distinct amts. of O6-MG were found in the latter animals. In contrast to the above-mentioned morphol. findings, no morphol. alterations occurred in the respiratory tract of the animals treated with NMBA alone. It is therefore conceivable that the above pathol. lesions resulted not merely from the presence of DNA adducts, but also from an addnl., previously unspecified effect. As benzaldehyde (BA) [100-52-7] is formed in equimolar amts. in NMBA metab. and DSF has been demonstrated to inhibit aldehyde metab., this aldehyde is a possible candidate for such an effect. In the present study, rats were therefore treated with BA, DSF, or NMBA, or combinations thereof. Long-term application of BA alone led to goblet cell hyperplasia, hyperplasia of the peribronchial lymphatic system, mucous epithelial atrophy, and accompanying perivasculitis - the same alterations seen under long-term application of NMBA and DSF. The changes were most pronounced in the group with concomitant application of NMBA, DSF, and BA. Apparently, BA plays a role in pathol. changes obsd. under the influence of NMBA.

ST disulfiram DNA benzaldehyde nitrosomethylbenzylamine carcinogenesis
IT Neoplasm
Papilloma
(from nitrosomethylbenzylamine, of respiratory tract, disulfiram effect on, mechanism of)
IT Deoxyribonucleic acids
RL: BIOL (Biological study)
(nitrosomethylbenzylamine adducts, of lung, disulfiram effect on, lung neoplasm in relation to)
IT Respiratory tract
(disease, metaplasia, from nitrosomethylbenzylamine, disulfiram effect on, mechanism of)
IT Respiratory tract
(neoplasm, from nitrosomethylbenzylamine, disulfiram effect on, mechanism of)

IT 100-52-7, Benzaldehyde, biological studies
RL: FORM (Formation, nonpreparative)
(formation of, from nitrosomethylbenzylamine, in lung, lung neoplasm in relation to)
IT 937-40-6, N-Nitroso-N-methylbenzylamine
RL: BIOL (Biological study)
(lung neoplasm induction by, disulfiram effect on, benzaldehyde in relation to)
IT **97-77-8**, Disulfiram
RL: BIOL (Biological study)
(nitrosomethylbenzylamine-induced lung neoplasm response to, benzaldehyde in relation to)
IT 20535-83-5
RL: BIOL (Biological study)
(of lung DNA, in nitrosomethylbenzylamine-induced lung neoplasm)

L49 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 1985:466487 HCAPLUS
DN 103:66487
TI Role of the respiratory system in metabolism of N-nitrosamines after simultaneous application of disulfiram
AU Buerkle, V.; Wittenberg, H.; Schweinsberg, F.; Weissenberger, I.; Schweinsberg, E.; Brueckner, B.
CS Pathol. Inst., Univ. Tuebingen, Tuebingen, Fed. Rep. Ger.
SO IARC Sci. Publ. (1984), 57(N-Nitroso Compd: Occurrence, Biol. Eff. Relevance Hum. Cancer), 533-41
CODEN: IARCCD; ISSN: 0300-5038
DT Journal
LA English
CC 4-6 (Toxicology)
AB Subsequent to modification of N-nitrosamines metab. by disulfiram [**97-77-8**], mucus-producing cells and Clara cells in the respiratory tract are involved increasingly in detoxification as well as in bioactivation of N-nitroso-N-methylbenzylamine [937-40-6] and N-nitrosodibutylamine [924-16-3]. Overtaxing of these cells or local concn. of antigenic metabolites leads to cytolytic defects in tracheal, bronchial, and bronchiolar epithelium, in addn. to toxic degenerative lesions. The resulting continuous stimulation of proliferation leads to basal-cell hyperplasia, squamous-cell metaplasia, and squamous **papillomas**. In areas with insufficient differentiation, due to cell proliferation, there is an increased probability that focal mutation, subsequent to alkylation of purine bases, will be passed from 1 cell generation to the next, with subsequent formation of tumors in the bronchioloalveolar region.
ST nitrosamine metab disulfiram neoplasm
IT Neoplasm
(from nitrosamine, of respiratory tract, disulfiram effect on)
IT Respiratory tract
(neoplasm, from nitrosamine, disulfiram effect on)
IT 924-16-3 937-40-6
RL: BIOL (Biological study)
(neoplasm from, of respiratory tract, disulfiram effect on)
IT **97-77-8**
RL: BIOL (Biological study)
(nitrosamine metab. response to, respiratory tract neoplasm in relation to)

L49 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 1984:585821 HCAPLUS
DN 101:185821
TI Induction of tumors of the nasal cavity in rats by concurrent feeding of thiram and sodium nitrite
AU Lijinsky, William

CS Chem. Carcinog. Lab., Natl. Cancer Inst., Frederick, MD, 21701, USA
SO J. Toxicol. Environ. Health (1984), 13(4-6), 609-14
CODEN: JTEHD6; ISSN: 0098-4108
DT Journal
LA English
CC 4-6 (Toxicology)
AB Simultaneous feeding to rats of thiram [**137-26-8**] with NaNO2 was carried out to assess the possibility of formation of carcinogenic N-nitroso derivs. in vivo. Following the administration of feed contg. 500 ppm thiram plus 2000 ppm NaNO2 for 104 wk, a high incidence of tumors of the nasal cavity was found in both sexes, 18 of 24 males and 15 of 24 females. No nasal cavity tumors were seen in untreated rats, or those given 500 ppm of thiram or 2000 ppm of NaNO2 alone. A 20% incidence of **papillomas** of the forestomach was also seen in the rats of both sexes given the combined treatment. The other significant difference in incidence of tumors between the rats given thiram with or without nitrite was a decreased no. of animals with monocytic leukemia, which is a common neoplasm in untreated F344 rats.
ST nose neoplasm thiram nitrite
IT **Papilloma**
(from sodium nitrite and thiram, of forestomach)
IT Neoplasm
(from sodium nitrite and thiram, of nasal cavity)
IT Nose
(neoplasm, from sodium nitrite and thiram)
IT **137-26-8**
RL: BIOL (Biological study)
(nasal cavity tumor induction by sodium nitrite and)
IT 7632-00-0
RL: BIOL (Biological study)
(nasal cavity tumor induction by thiram and)

L49 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 1982:47372 HCAPLUS
DN 96:47372
TI Effect of disulfiram on the toxicity and carcinogenicity of N-methyl-N-nitrosobenzylamine in rats
AU Schweinsberg, F; Buerkle, V.
CS Hyg. Inst., Univ. Tuebingen, Tuebingen, D-7400, Fed. Rep. Ger.
SO J. Cancer Res. Clin. Oncol. (1981), 102(1), 43-7
CODEN: JCROD7; ISSN: 0171-5216
DT Journal
LA German
CC 4-6 (Toxicology)
AB The simultaneous administration of 200 or 710 mg/kg diet of disulfiram [**97-77-8**] to female SIV 50 rats receiving 10 mg/L N-methyl-N-nitrosobenzylamine [937-40-6] in drinking water increased the toxicity of the latter markedly and accelerated the formation of esophageal tumors. Tracheal squamous cell **papillomas** and potentially precancerous squamous cell metaplasia in the bronchial system were found also.
ST methylnitrosobenzylamine carcinogenicity toxicity disulfiram; benzylamine methylnitroso carcinogenicity toxicity disulfiram
IT Neoplasm
(from methylnitrosobenzylamine, disulfiram effect on)
IT Esophagus
Trachea
(neoplasm, from methylnitrosobenzylamine, disulfiram effect on)
IT Bronchi
(neoplasms, from methylnitrosobenzylamine, disulfiram effect on)
IT 937-40-6
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(carcinogenicity and toxicity of, disulfiram effect on)

IT **97-77-8**
RL: BIOL (Biological study)
(methylnitrosobenzylamine carcinogenicity and toxicity response to)

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Calculated physical property data is now available. See HELP PROPERTIES
for more information. See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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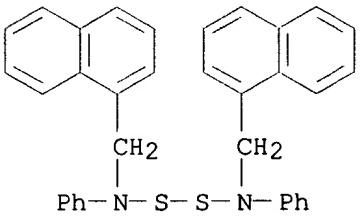
L50 ANSWER 1 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **320609-22-1** REGISTRY
CN 1-Naphthalenemethanamine, N,N'-dithiobis[N-phenyl- (9CI) (CA INDEX NAME)
MF C34 H28 N2 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Hit structures for rep 1-12, see L49

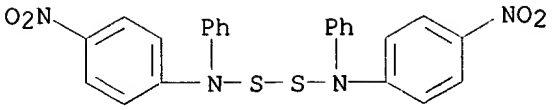


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 2 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **320609-21-0** REGISTRY
CN Benzenamine, N,N'-dithiobis[4-nitro-N-phenyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C24 H18 N4 O4 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



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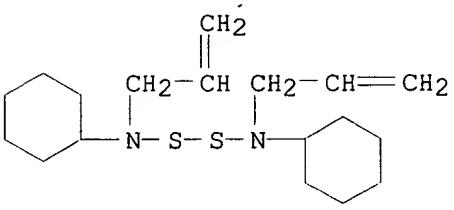
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 3 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **320609-19-6** REGISTRY
CN Cyclohexanamine, N,N'-dithiobis[N-2-propenyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C18 H32 N2 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

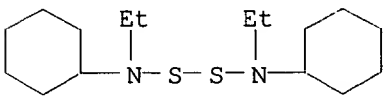


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 4 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **320609-18-5** REGISTRY
CN Cyclohexanamine, N,N'-dithiobis[N-ethyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C16 H32 N2 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



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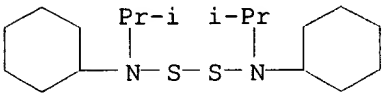
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 5 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **320609-17-4** REGISTRY
CN Cyclohexanamine, N,N'-dithiobis[N-(1-methylethyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C18 H36 N2 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



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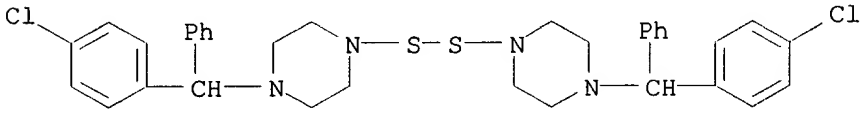
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 6 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **320609-16-3** REGISTRY
CN Piperazine, 1,1'-dithiobis[4-[(4-chlorophenyl)phenylmethyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C34 H36 Cl2 N4 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

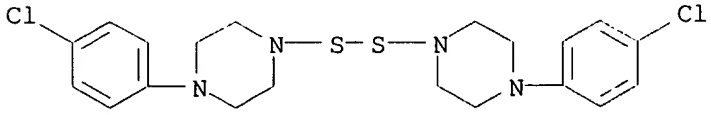


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 7 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **320609-15-2** REGISTRY
CN Piperazine, 1,1'-dithiobis[4-(4-chlorophenyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C20 H24 Cl2 N4 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

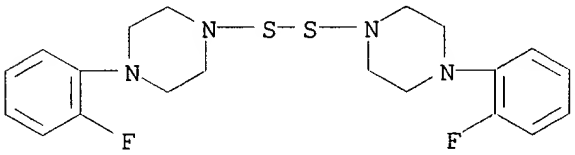


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 8 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **320609-14-1** REGISTRY
CN Piperazine, 1,1'-dithiobis[4-(2-fluorophenyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C20 H24 F2 N4 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

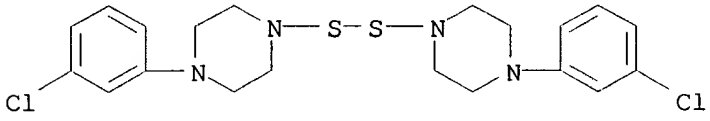


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 9 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **320609-13-0** REGISTRY
CN Piperazine, 1,1'-dithiobis[4-(3-chlorophenyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C20 H24 Cl2 N4 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

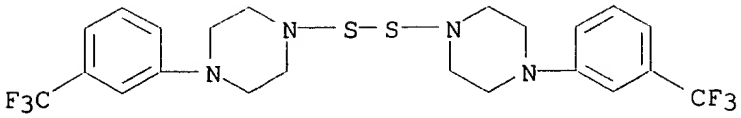


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 10 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **320609-12-9** REGISTRY
CN Piperazine, 1,1'-dithiobis[4-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C22 H24 F6 N4 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

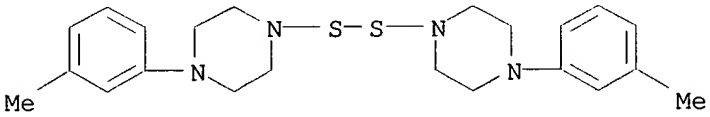


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 11 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **320609-11-8** REGISTRY
CN Piperazine, 1,1'-dithiobis[4-(3-methylphenyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C22 H30 N4 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

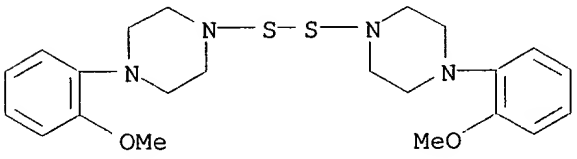


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 12 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **320609-10-7** REGISTRY
CN Piperazine, 1,1'-dithiobis[4-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C22 H30 N4 O2 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

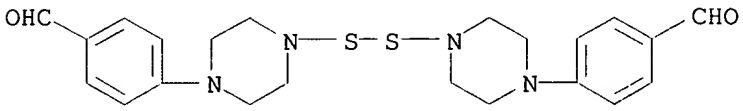


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 13 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **320609-09-4** REGISTRY
CN Benzaldehyde, 4,4'-(dithiodi-4,1-piperazinediyl)bis- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C22 H26 N4 O2 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

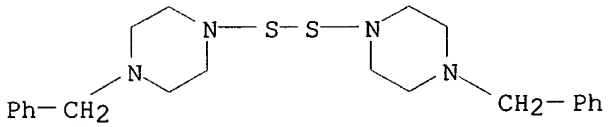


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 14 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **320609-08-3** REGISTRY
CN Piperazine, 1,1'-dithiobis[4-(phenylmethyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C22 H30 N4 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

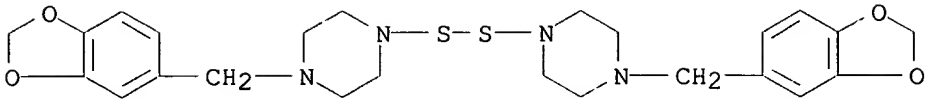


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 15 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **320609-07-2** REGISTRY
CN Piperazine, 1,1'-dithiobis[4-(1,3-benzodioxol-5-ylmethyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C24 H30 N4 O4 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

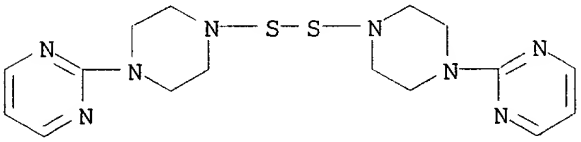


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 16 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **320609-06-1** REGISTRY
CN Pyrimidine, 2,2'-(dithiodi-4,1-piperazinediyl)bis- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C16 H22 N8 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

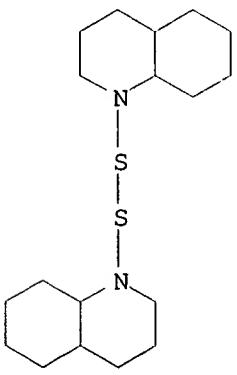


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 17 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **320609-05-0** REGISTRY
CN Quinoline, 1,1'-dithiobis[decahydro- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C18 H32 N2 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

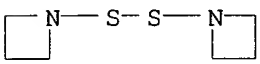


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 18 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **320609-04-9** REGISTRY
CN Azetidine, 1,1'-dithiobis- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C6 H12 N2 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

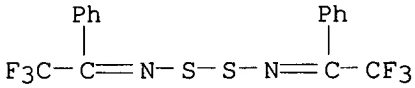


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 19 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **303796-55-6** REGISTRY
CN Benzenemethanimine, N,N'-dithiobis[.alpha.-(trifluoromethyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C16 H10 F6 N2 S2
SR Chemical Library
LC STN Files: CA, CAPLUS, CHEMCATS, TOXCENTER

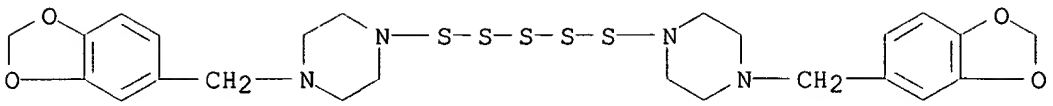


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 20 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **260973-87-3** REGISTRY
CN Piperazine, 1,1'-pentathiobis[4-(1,3-benzodioxol-5-ylmethyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C24 H30 N4 O4 S5
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

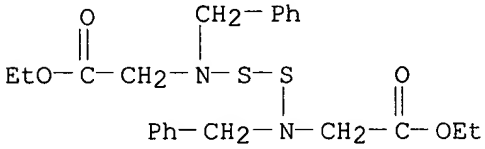


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:222549

L50 ANSWER 21 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **260973-85-1** REGISTRY
CN Glycine, N,N'-dithiobis[N-(phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C22 H28 N2 O4 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



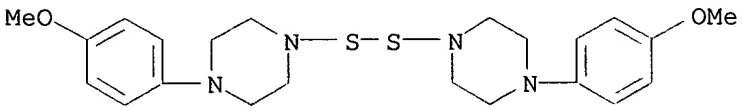
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

REFERENCE 2: 132:222549

L50 ANSWER 22 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **260973-83-9** REGISTRY
CN Piperazine, 1,1'-dithiobis[4-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C22 H30 N4 O2 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



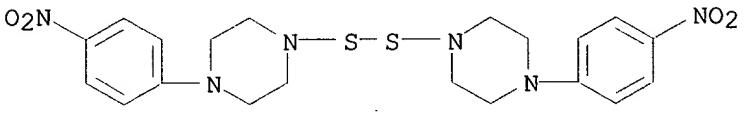
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

REFERENCE 2: 132:222549

L50 ANSWER 23 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **260973-81-7** REGISTRY
CN Piperazine, 1,1'-dithiobis[4-(4-nitrophenyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C20 H24 N6 O4 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



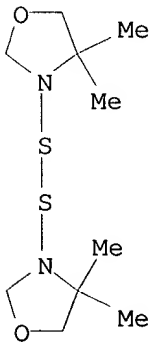
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

REFERENCE 2: 132:222549

L50 ANSWER 24 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **260973-79-3** REGISTRY
CN Oxazolidine, 3,3'-dithiobis[4,4-dimethyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C10 H20 N2 O2 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

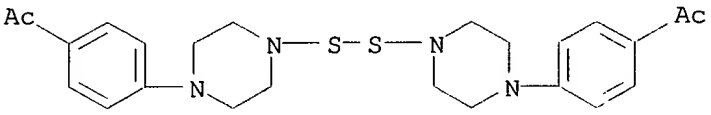
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

REFERENCE 2: 132:222549

L50 ANSWER 25 OF 50 REGISTRY COPYRIGHT 2002 ACS

RN **260973-76-0** REGISTRY
CN Ethanone, 1,1'-[dithiobis(4,1-piperazinediyl-4,1-phenylene)]bis- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C24 H30 N4 O2 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



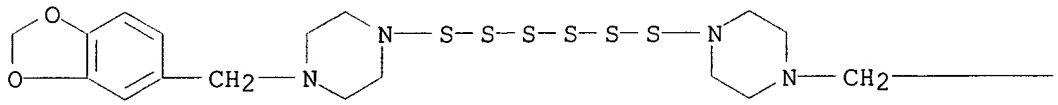
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

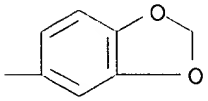
REFERENCE 1: 132:222549

L50 ANSWER 26 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **260973-75-9** REGISTRY
CN Piperazine, 1,1'-hexathiobis[4-(1,3-benzodioxol-5-ylmethyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C24 H30 N4 O4 S6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

PAGE 1-A



PAGE 1-B

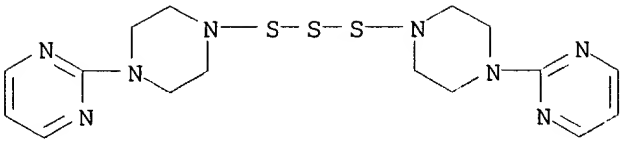


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:222549

L50 ANSWER 27 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **260973-74-8** REGISTRY
CN Pyrimidine, 2,2'-(trithiodi-4,1-piperazinediyl)bis- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C16 H22 N8 S3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

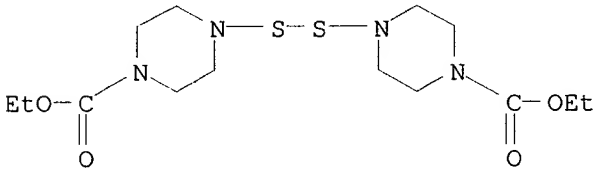


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:222549

L50 ANSWER 28 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **260973-72-6** REGISTRY
CN 1-Piperazinecarboxylic acid, 4,4'-dithiobis-, diethyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C14 H26 N4 O4 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



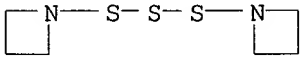
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

REFERENCE 2: 132:222549

L50 ANSWER 29 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **260973-68-0** REGISTRY
CN Azetidine, 1,1'-trithiobis- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C6 H12 N2 S3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

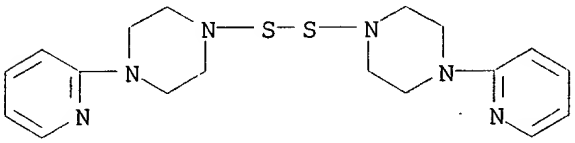


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:222549

L50 ANSWER 30 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **260973-66-8** REGISTRY
CN Piperazine, 1,1'-dithiobis[4-(2-pyridinyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C18 H24 N6 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



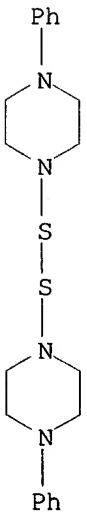
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

REFERENCE 2: 132:222549

L50 ANSWER 31 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **103388-17-6** REGISTRY
CN Piperazine, 1,1'-dithiobis[4-phenyl- (6CI, 9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C20 H26 N4 S2
SR CAOLD
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, TOXCENTER
(*File contains numerically searchable property data)



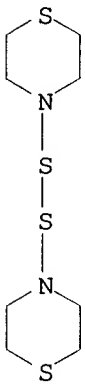
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)
4 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:110110

L50 ANSWER 32 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **98999-00-9** REGISTRY
CN Thiomorpholine, 4,4'-dithiobis- (6CI, 9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C8 H16 N2 S4
SR CAOLD
LC STN Files: CA, CAOLD, CAPLUS, TOXCENTER



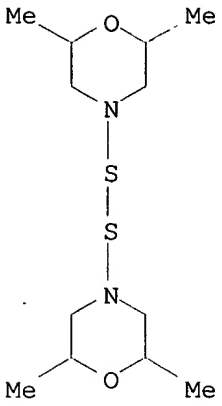
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:110110

REFERENCE 2: 132:222549

L50 ANSWER 33 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **85865-96-9** REGISTRY
CN Morpholine, 4,4'-dithiobis[2,6-dimethyl- (6CI, 9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C12 H24 N2 O2 S2
SR Commission of European Communities
LC STN Files: CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, TOXCENTER, USPATFULL
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

8 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
8 REFERENCES IN FILE CAPLUS (1967 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:110110

REFERENCE 2: 132:222549

REFERENCE 3: 123:345471

REFERENCE 4: 114:41666

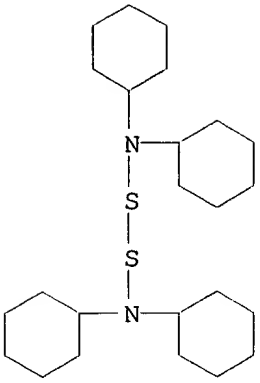
REFERENCE 5: 112:181185

REFERENCE 6: 112:58046

REFERENCE 7: 112:37910

REFERENCE 8: 111:98806

L50 ANSWER 34 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **72896-38-9** REGISTRY
CN Cyclohexanamine, N,N'-dithiobis[N-cyclohexyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C24 H44 N2 S2
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

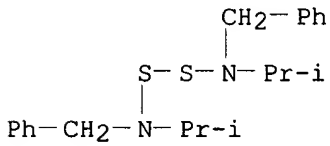
3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

REFERENCE 2: 99:25267

REFERENCE 3: 92:119716

L50 ANSWER 35 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **62158-06-9** REGISTRY
CN Benzenemethanamine, N,N'-dithiobis[N-(1-methylethyl)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN N,N'-Dithiobis[N-isopropylbenzylamine]
FS 3D CONCORD
MF C20 H28 N2 S2
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXCENTER
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

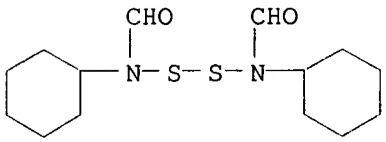
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

REFERENCE 2: 86:120244

L50 ANSWER 36 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **59226-72-1** REGISTRY
CN Formamide, N,N'-dithiobis[N-cyclohexyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C14 H24 N2 O2 S2

LC STN Files: BEILSTEIN*, CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

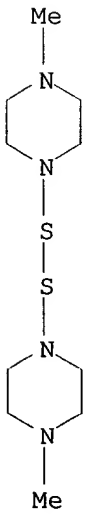
REFERENCE 1: 134:110110

REFERENCE 2: 132:222549

REFERENCE 3: 86:120883

REFERENCE 4: 84:179730

L50 ANSWER 37 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **36938-10-0** REGISTRY
CN Piperazine, 1,1'-dithiobis[4-methyl- (6CI, 7CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1,1'-Dithiobis[4-methylpiperazine]
CN Bis(4-methyl-1-piperazinyl) disulfide
CN Dithiobis[N-methylpiperazine]
FS 3D CONCORD
MF C10 H22 N4 S2
CI COM
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, RTECS*, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

10 REFERENCES IN FILE CA (1967 TO DATE)
10 REFERENCES IN FILE CAPLUS (1967 TO DATE)
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:110110

REFERENCE 2: 132:222549

REFERENCE 3: 127:347482

REFERENCE 4: 122:316653

REFERENCE 5: 122:108352

REFERENCE 6: 119:51087

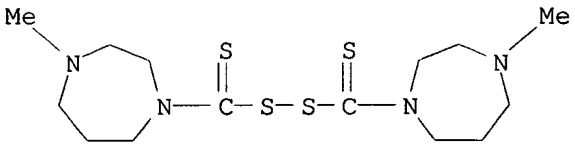
REFERENCE 7: 105:171948

REFERENCE 8: 99:25267

REFERENCE 9: 80:37060

REFERENCE 10: 77:63107

L50 ANSWER 38 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **26087-98-9** REGISTRY
CN 1H-1,4-Diazepine, 1,1'-(dithiodicarbonothioyl)bis[hexahydro-4-methyl-(9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Disulfide, bis[(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)thiocarbonyl] (8CI)
OTHER NAMES:
CN Bis(4-methyl-1-homopiperazinylthiocarbonyl) disulfide
CN FLA 63
FS 3D CONCORD
MF C14 H26 N4 S4
LC STN Files: BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CHEMCATS, CHEMLIST, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, MEDLINE, PHAR, PROMT, RTECS*, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

109 REFERENCES IN FILE CA (1967 TO DATE)
109 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

REFERENCE 2: 132:222549

REFERENCE 3: 125:127644

REFERENCE 4: 119:20007

REFERENCE 5: 118:188689

REFERENCE 6: 115:174663

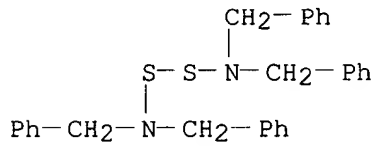
REFERENCE 7: 115:106556

REFERENCE 8: 114:178040

REFERENCE 9: 107:52640

REFERENCE 10: 107:664

L50 ANSWER 39 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **16131-50-3** REGISTRY
CN Benzenemethanamine, N,N'-dithiobis[N-(phenylmethyl)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Dibenzylamine, N,N'-dithiobis- (6CI, 8CI)
OTHER NAMES:
CN Dithiobis(dibenzylamine)
CN N,N'-Dithiobis(dibenzylamine)
MF C28 H28 N2 S2
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, CASREACT, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

9 REFERENCES IN FILE CA (1967 TO DATE)
9 REFERENCES IN FILE CAPLUS (1967 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:110110

REFERENCE 2: 127:347482

REFERENCE 3: 125:302994

REFERENCE 4: 122:316653

REFERENCE 5: 116:20620

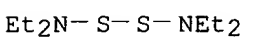
REFERENCE 6: 115:231541

REFERENCE 7: 115:221795

REFERENCE 8: 112:178823

REFERENCE 9: 111:146042

L50 ANSWER 40 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **15575-30-1** REGISTRY
CN Ethanamine, N,N'-dithiobis[N-ethyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Diethylamine, N,N'-dithiobis- (7CI, 8CI)
OTHER NAMES:
CN Bis(diethylamino) disulfide
CN Dithiobis[diethylamine]
CN N,N'-Dithiobis(diethylamine)
FS 3D CONCORD
DR 98543-47-6
MF C8 H20 N2 S2
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, CASREACT, CHEMINFORMRX, DETHERM*, IFICDB, IFIPAT, IFIUDB, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

23 REFERENCES IN FILE CA (1967 TO DATE)
23 REFERENCES IN FILE CAPLUS (1967 TO DATE)
8 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 136:262761

REFERENCE 2: 134:110110

REFERENCE 3: 132:222549

REFERENCE 4: 116:20620

REFERENCE 5: 115:221795

REFERENCE 6: 115:182227

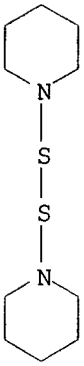
REFERENCE 7: 112:178823

REFERENCE 8: 107:217421

REFERENCE 9: 97:39023

REFERENCE 10: 94:183348

L50 ANSWER 41 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **10220-20-9** REGISTRY
CN Piperidine, 1,1'-dithiobis- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Piperidine, 1,1'-dithiodi- (6CI, 7CI, 8CI)
OTHER NAMES:
CN 1,1'-Dithiodipiperidine
CN Dipiperidino disulfide
CN N,N'-Dithiobis(piperidine)
FS 3D CONCORD
MF C10 H20 N2 S2
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CSCHEM, GMELIN*, HODOC*, IFICDB, IFIPAT, IFIUDB, RTECS*, SPECINFO, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

49 REFERENCES IN FILE CA (1967 TO DATE)
49 REFERENCES IN FILE CAPLUS (1967 TO DATE)
14 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 137:73255

REFERENCE 2: 134:110110

REFERENCE 3: 132:222549

REFERENCE 4: 126:143785

REFERENCE 5: 126:18633

REFERENCE 6: 120:164086

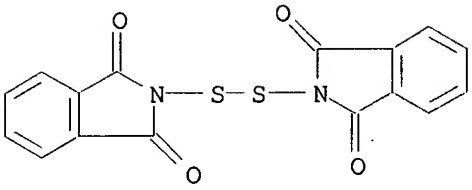
REFERENCE 7: 116:20620

REFERENCE 8: 115:231541

REFERENCE 9: 115:221795

REFERENCE 10: 113:211924

L50 ANSWER 42 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **7764-30-9** REGISTRY
CN 1H-Isoindole-1,3(2H)-dione, 2,2'-dithiobis- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Phthalimide, N,N'-dithiodi- (7CI)
OTHER NAMES:
CN N,N'-Dithiobis(phthalimide)
FS 3D CONCORD
MF C16 H8 N2 O4 S2
CI COM
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, GMELIN*, IFICDB, IFIPAT, IFIUDB, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

26 REFERENCES IN FILE CA (1967 TO DATE)
26 REFERENCES IN FILE CAPLUS (1967 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 137:70673

REFERENCE 2: 135:53776

REFERENCE 3: 134:110110

REFERENCE 4: 132:222549

REFERENCE 5: 127:66018

REFERENCE 6: 123:112220

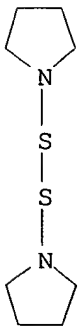
REFERENCE 7: 115:255749

REFERENCE 8: 114:206663

REFERENCE 9: 109:242969

REFERENCE 10: 109:54039

L50 ANSWER 43 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **6542-61-6** REGISTRY
CN Pyrrolidine, 1,1'-dithiobis- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Pyrrolidine, 1,1'-dithiodi- (7CI, 8CI)
OTHER NAMES:
CN 1-Pyrrolidinyl disulfide
FS 3D CONCORD
MF C8 H16 N2 S2
CI COM
LC STN Files: CA, CAOLD, CAPLUS, TOXCENTER



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

6 REFERENCES IN FILE CA (1967 TO DATE)
6 REFERENCES IN FILE CAPLUS (1967 TO DATE)
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:110110

REFERENCE 2: 132:222549

REFERENCE 3: 117:183804

REFERENCE 4: 114:41666

REFERENCE 5: 94:183348

REFERENCE 6: 84:89215

L50 ANSWER 44 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **2129-27-3** REGISTRY
CN Benzenamine, N,N'-dithiobis[N-phenyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Diphenylamine, N,N'-dithiobis- (7CI)
OTHER NAMES:
CN Bis(diphenylamino) disulfide
FS 3D CONCORD
MF C24 H20 N2 S2
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

$Ph_2N-S-S-NPh_2$

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1967 TO DATE)
5 REFERENCES IN FILE CAPLUS (1967 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:110110

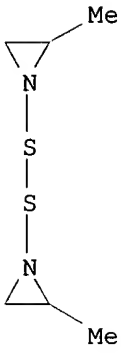
REFERENCE 2: 94:183348

REFERENCE 3: 92:119716

REFERENCE 4: 89:107376

REFERENCE 5: 84:89215

L50 ANSWER 45 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **1623-85-4** REGISTRY
CN Aziridine, 1,1'-dithiobis[2-methyl- (7CI, 8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN ENT 50361
FS 3D CONCORD
MF C6 H12 N2 S2
LC STN Files: CA, CAOLD, CAPLUS, TOXCENTER



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

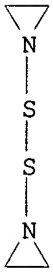
3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)
4 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:110110

REFERENCE 2: 132:222549

REFERENCE 3: 70:10608

L50 ANSWER 46 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **1623-84-3** REGISTRY
CN Aziridine, 1,1'-dithiobis- (7CI, 8CI, 9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C4 H8 N2 S2
CI COM
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, TOXCENTER
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

6 REFERENCES IN FILE CA (1967 TO DATE)
6 REFERENCES IN FILE CAPLUS (1967 TO DATE)
8 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:110110

REFERENCE 2: 132:222549

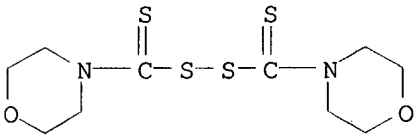
REFERENCE 3: 115:122307

REFERENCE 4: 70:10608

REFERENCE 5: 69:35917

REFERENCE 6: 67:90726

L50 ANSWER 47 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **729-46-4** REGISTRY
CN Morpholine, 4,4'-(dithiodicarbonothioyl)bis- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Disulfide, bis(morpholinothiocarbonyl) (6CI, 7CI, 8CI)
OTHER NAMES:
CN 4-Morpholinethiocarbonyl disulfide
CN Bis(4-morpholinethiocarbonyl) disulfide
CN Bis(morpholinothiocarbonyl) disulfide
CN Dimorpholinethiuram disulfide
CN Disulfide, bis(4-morpholinylthioxomethyl)
CN NSC 402538
CN Thiuram disulfide, bis(oxydi-2,1-ethanediyl)-
FS 3D CONCORD
MF C10 H16 N2 O2 S4
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, GMELIN*, IFICDB, IFIPAT, IFIUDB, RTECS*, SPECINFO, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

63 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
63 REFERENCES IN FILE CAPLUS (1967 TO DATE)
18 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 136:184061

REFERENCE 2: 134:237436

REFERENCE 3: 134:110110

REFERENCE 4: 133:222350

REFERENCE 5: 132:222549

REFERENCE 6: 132:59191

REFERENCE 7: 129:92767

REFERENCE 8: 125:184901

REFERENCE 9: 124:29364

REFERENCE 10: 122:186597

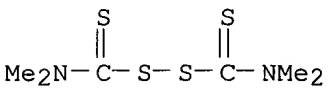
L50 ANSWER 48 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **137-26-8** REGISTRY
CN Thioperoxydicarbonic diamide ([(H2N)C(S)]2S2), tetramethyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Disulfide, bis(dimethylthiocarbamoyl) (8CI)
OTHER NAMES:
CN AApirol
CN Aatiram
CN Accel TMT
CN Accelerant T
CN Accelerator T
CN Accelerator Thiuram
CN Aceto TETD
CN Anles
CN Arasan
CN Arasan 42S
CN Arasan 50 red
CN Arasan 70
CN Arasan 70-S Red
CN Arasan 75
CN Arasan M
CN Arasan-SF
CN Atiram
CN Basultra
CN Betoxin
CN Bis(dimethylthiocarbamoyl) disulfide
CN Bis(dimethylthiocarbamyl) disulfide
CN Cunitex
CN Delsan
CN Ekagom TB
CN Emol
CN Falitiram
CN Ferna-Col
CN Fernasan
CN Fernasan A
CN Fernide
CN Formalsol
CN Hermal
CN Hermat TMT
CN Heryl
CN Hexathir
CN Kregasan
CN Mercuram
CN Methyl Thiram
CN Methyl Tuads
CN Metiur
CN Metiurac
CN N,N,N',N'-Tetramethylthiuram disulfide
CN Nobecutan
CN Nocceler TT
CN Normersan
CN NSC 1771
CN Orac TMTD
CN Panoram 75
CN Perkacit TMTD
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
FS 3D CONCORD
DR 12680-07-8, 12680-62-5, 56645-31-9, 66173-72-6, 93196-73-7, 39456-80-9
MF C6 H12 N2 S4
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,

BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHARMASEARCH, PIRA, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL, VETU

(*File contains numerically searchable property data)

Other Sources: DSL**, EINECS**, TSCA**, WHO

(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5345 REFERENCES IN FILE CA (1967 TO DATE)
90 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
5347 REFERENCES IN FILE CAPLUS (1967 TO DATE)
51 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 137:83098

REFERENCE 2: 137:80050

REFERENCE 3: 137:74595

REFERENCE 4: 137:64352

REFERENCE 5: 137:59004

REFERENCE 6: 137:47787

REFERENCE 7: 137:35457

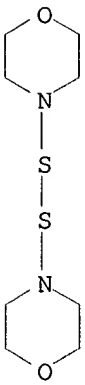
REFERENCE 8: 137:34375

REFERENCE 9: 137:34370

REFERENCE 10: 137:16590

L50 ANSWER 49 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **103-34-4** REGISTRY
CN Morpholine, 4,4'-dithiobis- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Morpholine, 4,4'-dithiodi- (6CI, 7CI, 8CI)
OTHER NAMES:
CN 4,4'-Dithiobis[morpholine]
CN 4,4'-Dithiodimorpholine
CN Accel R
CN Bismorpholine disulfide
CN Bismorpholino disulfide
CN Deovulc M
CN Di(4-morpholinyl) disulfide
CN DTDM
CN Morpholine disulfide
CN Morpholinodisulfide
CN N,N'-Bismorpholine disulfide
CN N,N'-Dimorpholinyl disulfide
CN N,N'-Dithiobis[morpholine]

CN N,N'-Dithiodimorpholine
CN Rhenocure M/G
CN Sanfel R
CN Sulfasan
CN Sulfasan DTDM
CN Sulfasan R
CN Vanax A
CN Vulnoc R
FS 3D CONCORD
DR 39393-19-6
MF C8 H16 N2 O2 S2
CI COM
LC STN Files: BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, EMBASE, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PROMT, RTECS*, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

502 REFERENCES IN FILE CA (1967 TO DATE)
5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
503 REFERENCES IN FILE CAPLUS (1967 TO DATE)
42 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 137:73255

REFERENCE 2: 137:35409

REFERENCE 3: 137:34375

REFERENCE 4: 137:34370

REFERENCE 5: 136:388294

REFERENCE 6: 136:341988

REFERENCE 7: 136:329488

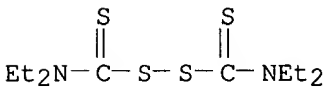
REFERENCE 8: 136:329305

REFERENCE 9: 136:327942

REFERENCE 10: 136:262761

L50 ANSWER 50 OF 50 REGISTRY COPYRIGHT 2002 ACS
RN **97-77-8** REGISTRY
CN Thioperoxydicarbonic diamide ([(H2N)C(S)]2S2), tetraethyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Disulfide, bis(diethylthiocarbamoyl) (8CI)
OTHER NAMES:
CN Abstensil
CN Abstinil
CN Abstinyl
CN Accel TET
CN Accel TET-R
CN Alcophobin
CN Antabus
CN Antabuse
CN Antadix
CN Antaethyl
CN Antalcol
CN Antetan
CN Antetil
CN Anticol
CN Antietanol
CN Antietil
CN Antikol
CN Antivitium
CN Aversan
CN Averzan
CN Bis(diethylthiocarbamoyl) disulfide
CN Bis(N,N-diethylthiocarbamoyl) disulfide
CN Contralin
CN Cronetal
CN Dicupral
CN Disulfiram
CN Ekagom DTET
CN Ekagom TEDS
CN Ekagom TETDS
CN Espenal
CN Esperal
CN Etabus
CN Ethyl Thiram
CN Ethyl Thiurad
CN Ethyl Tuads
CN Ethyl Tuex
CN Exhorran
CN Hoca
CN Krotenal
CN N,N,N',N'-Tetraethylthiuram disulfide
CN Nocceler TET
CN Nocceler TET-G
CN Noxal
CN NSC 25953
CN Refusal
CN Sanceler TET
CN Sanceler TET-G
CN Soxinol TET
CN Stopetyl
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
FS 3D CONCORD
DR 11078-22-1, 155-01-1
MF C10 H20 N2 S4

CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, DRUGUPDATES, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHARMASEARCH, PROMT, RTECS*, SPECINFO, TOXCENTER, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2152 REFERENCES IN FILE CA (1967 TO DATE)
42 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2156 REFERENCES IN FILE CAPLUS (1967 TO DATE)
23 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 137:74566

REFERENCE 2: 137:73615

REFERENCE 3: 137:63538

REFERENCE 4: 137:47787

REFERENCE 5: 137:34375

REFERENCE 6: 137:1669

REFERENCE 7: 136:402082

REFERENCE 8: 136:384227

REFERENCE 9: 136:379617

REFERENCE 10: 136:359716

L8 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1964:464408 CAPLUS
DOCUMENT NUMBER: 61:64408
ORIGINAL REFERENCE NO.: 61:11193e-f
TITLE: Development and application of fungistatic compounds for treatment of **cancer**
AUTHOR(S): Nieper, Hans A.; Xalabarder, Conrado
CORPORATE SOURCE: Krankenhaus, Aschaffenburg, Germany
SOURCE: Aerztl. Forsch. (1962), 16, I/523-I/540
DOCUMENT TYPE: Journal
LANGUAGE: German

AB The fungistatic substances were first tested in vitro on fungi and yeasts, esp. on Candida tropicalis, then on **tumors** (Ehrlich ascites carcinoma) and on **tumor** cells. Compds. contg. hydroxymethyl groups, ethylenimine groups, and S were compared for their effectiveness as antioncogenic agents. Trioxymethyl melanin proved still to be a most effective agent. Synthetic bis(hydroxymethylthiocarbamoyl) disulfide (LK 92) and compds. of related structure gave promising results.

IT Neoplasms
(inhibitors of, fungicides as)

IT Disulfide, bis[(3-carboxypiperidino)thiocarbonyl](?)
Glucitol, 1,1'-[dithiobis[(thiocarbonyl)(methylimino)]]bis[1-deoxy-
Thiuram disulfide bis(arginyl)-, bis(glucosamine)-
Thiuram disulfide bis(arginyl)-, bis(hydroxymethyl)-
(as neoplasm inhibitor)

IT 94-37-1, Disulfide, bis(piperidinothiocarbonyl) **729-46-4**, Disulfide, bis(morpholinothiocarbonyl) 3562-31-0, Disulfide, bis[(hydroxymethyl)thiocarbamoyl] 4310-59-2, D-Glucose, 2,2'-[dithiobis[(thiocarbonyl)imino]]bis[2-deoxy- 90114-66-2, Disulfide, bis[methyl(D-gluco-2,3,4,5,6-pentahydroxyhexyl)thiocarbamoyl] 93896-57-2, Nipecotic acid, 1,1'-[dithiobis(thiocarbonyl)]di-(?) 97771-69-2, Disulfide, bis[methyl(2-morpholinoethyl)thiocarbamoyl]
(as neoplasm inhibitor)

IT 1017-56-7, Methanol, (s-triazine-2,4,6-triyltriimino)tri-
(neoplasm inhibition and)

L8 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:507293 CAPLUS
DOCUMENT NUMBER: 132:87659
TITLE: Potential drugs against **cervical cancer**: zinc-ejecting inhibitors of the human **papillomavirus** type 16 E6 oncoprotein
AUTHOR(S): Beerheide, Walter; Bernard, Hans-Ulrich; Tan, Yee-Joo; Ganesan, Arasu; Rice, William G.; Ting, Anthony E.
CORPORATE SOURCE: Screening for Novel Inhibitors Laboratory, Institute of Molecular and Cell Biology, Singapore, 117609, Singapore
SOURCE: Journal of the National Cancer Institute (1999), 91(14), 1211-1220
CODEN: JNCIEQ; ISSN: 0027-8874
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The principal agent in the etiol. of **cervical cancer**, i.e., human **papillomavirus** (**HPV**) type 16, encodes three oncoproteins, E5, E6, and E7. Structural and mutational studies have identified two potential zinc-finger domains as crit. for E6 protein function. We investigated several assays to identify and characterize compds. that interfere with the binding of zinc to E6. Thirty-six compds. were selected on the basis of their structure, which would facilitate their participation in sulfhydryl residue-specific redox reactions, and were tested for their ability to release zinc from E6 protein. The zinc-ejecting compds. were then tested for their ability to inhibit E6 binding to E6-assocd. protein (E6AP) and E6-binding protein (E6BP), two coactivators of E6-mediated cellular transformation. The binding of E6 to E6BP and E6AP was measured by use of surface plasmon resonance (a technique that monitors mol. interactions by measuring changes in refractive index) and by use of in vitro translation assays. The compds. were also tested for their effects on the viability of **HPV** -contg. cell lines. Nine of the 36 tested compds. ejected zinc from E6. Two of the nine compds. inhibited the interaction of E6 with E6AP and E6BP, and one of these two, 4,4'-dithiodimorpholine, selectively inhibited cell viability and induced higher levels of p53 protein (assocd. with the induction of apoptosis [programmed cell death]) in tumorigenic **HPV** -contg. cells. We have described assay systems to identify compds., such as 4,4'-dithiodimorpholine, that can potentially interfere with the biol. and pathol. of **HPV**. These assay systems may be useful in the development of drugs against **cervical cancer**, genital **warts**, and asymptomatic infections by genital **HPVs**.
IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(E5; potential drugs against **cervical cancer**)
IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(E6; potential drugs against **cervical cancer**)
IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(E7; potential drugs against **cervical cancer**)
IT Antiviral agents
(anti- **HPV**; potential drugs against **cervical cancer**)
IT Uterus, neoplasm
Uterus, neoplasm
(cervix, inhibitors; potential drugs against **cervical cancer**)

IT Antitumor agents
(cervix; potential drugs against **cervical cancer**)
IT Analysis
Apoptosis
Drug design
Drug screening
Human **papillomavirus**
Redox reaction
(potential drugs against **cervical cancer**)
IT p53 (protein)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(potential drugs against **cervical cancer**)
IT Fusion proteins (chimeric proteins)
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(potential drugs against **cervical cancer**)
IT 56-17-7, Cystamine dihydrochloride 56-89-3, Cystine, analysis 69-78-3 97-77-8, Tetraethylthiuram disulfide 100-32-3 103-33-3, Azobenzene **103-34-4** 119-80-2 120-78-5, 2,2'-Dithiobis(benzothiazole) 123-77-3, Azodicarbonamide 135-57-9, Bis(2-benzamidophenyl)disulfide 150-60-7, Dibenzyl disulfide 537-91-7, Bis(3-Nitrophenyl)disulfide 586-96-9, Nitrosobenzene 644-32-6, Benzoyl disulfide 870-93-9, DL-Homocystine 882-33-7, Phenyl disulfide 940-69-2, .alpha.-Lipoamide 1141-88-4, 2,2'-Dithiodianiline 1155-00-6, Bis(2-nitrophenyl)disulfide 1160-68-5 2127-03-9, Aldrithiol 2 5398-51-6 13895-38-0, 4-Nitrosoresorcinol-1-monomethyl ether 15441-06-2, 3,3'-Dithiodipropionic acid dimethyl ester 16766-09-9, Bis(4-Acetamidophenyl)disulfide 26907-82-4 47231-30-1 108872-98-6 120586-49-4, 1,2-Dithiane-4,5-diol, 1,1-dioxide, cis 207802-09-3
RL: ANT (Analyte); ANST (Analytical study)
(potential drugs against **cervical cancer**)
IT 7440-66-6, Zinc, biological studies 50812-37-8, Glutathione S-transferase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(potential drugs against **cervical cancer**)
REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:175791 CAPLUS
DOCUMENT NUMBER: 132:222549
TITLE: Preparation of bis(piperazinyl) disulfides and analogs for treatment of **papillomavirus**-mediated disorders
INVENTOR(S): Bernard, Hans-Ulrich; Tan, Yee Joo; Beerheide, Walter; Ting, Anthony Eugene; Sim, Mui Mui
PATENT ASSIGNEE(S): Institute of Molecular & Cell Biology, Singapore; Hughes, E. John L.
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000014063	A1	20000316	WO 1999-AU724	19990903
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2342858	AA	20000316	CA 1999-2342858	19990903
AU 9958401	A1	20000327	AU 1999-58401	19990903
EP 1112250	A1	20010704	EP 1999-945758	19990903
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002524442	T2	20020806	JP 2000-568822	19990903

PRIORITY APPLN. INFO.:
AU 1998-5733 A 19980904
AU 1999-1645 A 19990715
WO 1999-AU724 W 19990903

OTHER SOURCE(S): MARPAT 132:222549

AB R1R2NZSSnZNR3R4 (I) [R1-R4 = H, alkyl, acyl, aryl, etc.; R1R2,R3R4 = (CH2)lUm(CH2)p; U = bond, O, S, NH, CH2; Z = bond or where n = 1 Z may = CS; l,p = 0-6; m = 0 or 1; l+m+p.gtoreq.2; n = 1-5], inhibitors of proteins encoded by an **MPV** gene by disruption of a chelated metal cation domain, were prepd. Thus, e.g., R1R2NSSNR3R4 (R1R2,R3R4 = CH2CH2NRCH2CH2, R = 2-pyridinyl) was prepd. Data for biol. activity of I were given.

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(E6; prepn. of bis(piperazinyl) disulfides and analogs for treatment of **papillomavirus**-mediated disorders)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(E7; prepn. of bis(piperazinyl) disulfides and analogs for treatment of **papillomavirus**-mediated disorders)

IT Uterus, neoplasm
Uterus, neoplasm
(cervix, inhibitors; prepn. of bis(piperazinyl) disulfides and analogs for treatment of **papillomavirus**-mediated disorders)

IT Antitumor agents

(cervix; prepn. of bis(piperazinyl) disulfides and analogs for treatment of **papillomavirus**-mediated disorders)

IT Transforming proteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibitors; prepn. of bis(piperazinyl) disulfides and analogs for treatment of **papillomavirus**-mediated disorders)

IT Human **papillomavirus** 16
Human **papillomavirus** 18
Papillomavirus
(prepn. of bis(piperazinyl) disulfides and analogs for treatment of **papillomavirus**-mediated disorders)

IT **103-34-4P 729-46-4P 1623-84-3P**
1623-85-4P 2759-28-6DP, N-Benzylpiperazine, 4,4'-polythiobis deriv. **6542-61-6P** 7764-30-9P **10220-20-9P**
15575-30-1P 26087-98-9P 35386-24-4DP, 1-(2-Methoxyphenyl)piperazine, 4,4'-polythiobis deriv. **36938-10-0P**
59226-72-1P 85865-96-9P 98999-00-9P
260973-66-8P 260973-68-0P **260973-72-6P** 260973-74-8P
260973-75-9P 260973-76-0P **260973-79-3P 260973-81-7P**
260973-83-9P 260973-85-1P 260973-87-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of bis(piperazinyl) disulfides and analogs for treatment of **papillomavirus**-mediated disorders)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:840664 CAPLUS
DOCUMENT NUMBER: 134:110110
TITLE: Inactivation of the human **papillomavirus**-16 E6 oncoprotein by organic disulfides
AUTHOR(S): Beerheide, Walter; Sim, Mui Mui; Tan, Yee-Joo; Bernard, Hans-Ulrich; Ting, Anthony E.
CORPORATE SOURCE: Drug Screen Development Laboratory, Institute of Molecular and Cell Biology, Singapore, 117609, Singapore
SOURCE: Bioorganic & Medicinal Chemistry (2000), 8(11), 2549-2560
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We are investigating compds. that could be useful in the treatment of neoplastic **lesions** of the cervix by acting on the oncoprotein E6 of human **papillomavirus**-16. The E6 protein contains two potential zinc-binding domains that are required for most of its functions. We have published tests that measure (i) the release of zinc ions after chem. alteration of the cysteine groups of these zinc-binding domains (TSQ assay), (ii) the interaction of E6 with the cellular proteins E6AP and E6BP (BIACORE assay), and (iii) the viability of **tumor** cell lines that require the continuous expression of **HPV** oncoproteins (WST1 assay). Based on these tests, we identified 4,4'-dithiodimorpholine as a potential lead compd. In this study we examd. whether the dithiobisamine moiety of 4,4'-dithiodimorpholine may be an important mol. prerequisite for further drug development in this system. We have evaluated 59 new substances including org. disulfides and those contg. the dithiobisamine moiety, as well as structural analogs. The compds. with significant reactivity in all three assays were obsd. only for dithiobisamine derivs. with satd. cyclic amines and aryl substituted piperazines. The identity of these substances suggests that the N-S-S-N moiety is necessary but not sufficient for reactivity in our assays, and that dithiobisamine based substances are useful as lead compds. that target the cysteine groups of **HPV**-16 E6 zinc fingers.

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(E6; prepn. of org. disulfides and inactivation of human **papillomavirus**-16 E6 oncoprotein)

IT Uterus, neoplasm
(cervix, inhibitors; prepn. of org. disulfides and inactivation of human **papillomavirus**-16 E6 oncoprotein)

IT Antitumor agents
(cervix; prepn. of org. disulfides and inactivation of human **papillomavirus**-16 E6 oncoprotein)

IT Human **papillomavirus** 16
Structure-activity relationship
(prepn. of org. disulfides and inactivation of human **papillomavirus**-16 E6 oncoprotein)

IT Amines, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(secondary; prepn. of org. disulfides and inactivation of human **papillomavirus**-16 E6 oncoprotein)

IT Protein motifs
(zinc-binding domain; prepn. of org. disulfides and inactivation of human **papillomavirus**-16 E6 oncoprotein)

IT **729-46-4P** 1013-93-0P 1468-28-6P **2129-27-3P**

5328-68-7P **6542-61-6P** 7764-30-9P **10220-20-9P**
15575-30-1P 16131-50-3P 17376-42-0P 36903-85-2P
36938-10-0P 59226-72-1P 62158-06-9P
72896-38-9P 85865-96-9P 98999-00-9P
103388-17-6P 260973-66-8P 260973-72-6P
260973-79-3P 260973-81-7P 260973-83-9P
260973-85-1P 303796-55-6P 320609-04-9P **320609-05-0P**
320609-06-1P 320609-07-2P 320609-08-3P
320609-09-4P 320609-10-7P 320609-11-8P
320609-12-9P 320609-13-0P 320609-14-1P **320609-15-2P**
320609-16-3P 320609-17-4P 320609-18-5P
320609-19-6P 320609-21-0P 320609-22-1P
320609-23-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of org. disulfides and inactivation of human **papillomavirus**-16 E6 oncoprotein)

IT **103-34-4** 120-78-5 880-09-1 **1623-84-3**
1623-85-4 2127-10-8 2550-40-5 3256-06-2,
Thioperoxydicarbonimidic diamide ([(H2N)C(NH)]2S2) 5117-07-7
14193-38-5 15658-35-2 **26087-98-9** 61747-35-1 66304-01-6
66546-28-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of org. disulfides and inactivation of human **papillomavirus**-16 E6 oncoprotein)

IT 85-46-1, Naphthalene-1-sulfonyl chloride 98-88-4, Benzoyl chloride
110-91-8, Morpholine, reactions 1122-82-3, Cyclohexyl isothiocyanate
6160-65-2, 1,1'-Thiocarbonyl diimidazole 7693-46-1, 4-Nitrophenyl chloroformate 10025-67-9, Disulfur dichloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of org. disulfides and inactivation of human **papillomavirus**-16 E6 oncoprotein)

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2003 ACS

L8 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2003 ACS

AB We are investigating compds. that could be useful in the treatment of neoplastic **lesions** of the cervix by acting on the oncoprotein E6 of human **papillomavirus**-16. The E6 protein contains two potential zinc-binding domains that are required for most of its functions. We have published tests that measure (i) the release of zinc ions after chem. alteration of the cysteine groups of these zinc-binding domains (TSQ assay), (ii) the interaction of E6 with the cellular proteins E6AP and E6BP (BIACORE assay), and (iii) the viability of **tumor** cell lines that require the continuous expression of **HPV** oncoproteins (WST1 assay). Based on these tests, we identified 4,4'-dithiodimorpholine as a potential lead compd. In this study we examd. whether the dithiobisamine moiety of 4,4'-dithiodimorpholine may be an important mol. prerequisite for further drug development in this system. We have evaluated 59 new substances including org. disulfides and those contg. the dithiobisamine moiety, as well as structural analogs. The compds. with significant reactivity in all three assays were obsd. only for dithiobisamine derivs. with satd. cyclic amines and aryl substituted piperazines. The identity of these substances suggests that the N-S-S-N moiety is necessary but not sufficient for reactivity in our assays, and that dithiobisamine based substances are useful as lead compds. that target the cysteine groups of **HPV**-16 E6 zinc fingers.

ACCESSION NUMBER: 2000:840664 CAPLUS
DOCUMENT NUMBER: 134:110110
TITLE: Inactivation of the human **papillomavirus**-16 E6 oncoprotein by organic disulfides
AUTHOR(S): Beerheide, Walter; Sim, Mui Mui; Tan, Yee-Joo; Bernard, Hans-Ulrich; Ting, Anthony E.
CORPORATE SOURCE: Drug Screen Development Laboratory, Institute of Molecular and Cell Biology, Singapore, 117609, Singapore
SOURCE: Bioorganic & Medicinal Chemistry (2000), 8(11), 2549-2560
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

RE

(1) Barbosa, M; Oncogene 1989, V4, P1529 CAPLUS
(2) Beerheide, W; J Natl Cancer Inst 1999, V91, P1211 CAPLUS
(3) Borch, R; Proc Natl Acad Sci 1979, V76, P6611 CAPLUS
(4) Butz, K; Oncogene 1995, V10, P927 CAPLUS
(5) Chan, S; J Virol 1995, V69, P3074 CAPLUS
(6) Chen, J; Science 1995, V269, P529 CAPLUS
(7) Crook, T; Cell 1991, V67, P547 CAPLUS
(8) Diaz, C; Phosphorus, Sulfur, and Silicon 1989, V44, P1
(9) Dyson, N; Science 1989, V243, P934 CAPLUS
(10) Frank, N; Toxicology 1995, V95, P113 CAPLUS
(11) Fritsche, M; Oncogene 1993, V8, P307 CAPLUS
(12) Gao, Q; Mol Cell Biol 1999, V19, P733 CAPLUS
(13) Gross-Mesilaty, S; Proc Natl Acad Sci 1998, V95, P8058 CAPLUS
(14) Grossman, S; Oncogene 1989, V4, P1089 CAPLUS
(15) Hathout, Y; Drug Metab Dispos 1996, V24, P1395 CAPLUS
(16) Huibregtse, J; Mol Cell Biol 1993, V13, P775 CAPLUS
(17) International Agency for Research on Cancer; IARC Monographs on the evaluation of carcinogenic risks to humans 1995, V64
(18) Katritzky, A; SYNLETT 1990, V8, P473
(19) Keys, H; N Engl J Med 1999, V340, P1154 CAPLUS
(20) Kovacich, J; J Thorac Cardiovasc Surg 1999, V118, P154 CAPLUS

(21) Kukimoto, I; Biochem Biophys Res Commun 1998, V249, P258 CAPLUS
(22) Lamberti, C; EMBO J 1990, V9, P1907 CAPLUS
(23) Liu, G; Mol Carcinog 1998, V22, P235 CAPLUS
(24) Liu, Y; J Virol 1999, V73, P7297 CAPLUS
(25) Malmqvist, M; Curr Opin Immunol 1993, V5, P282 CAPLUS
(26) Morris, M; N Engl J Med 1999, V340, P1137 MEDLINE
(27) Myers, G; Human Papillomaviruses 1995, P47
(28) Osswald, H; J Cancer Res Clin Oncol 1990, V116, P448 MEDLINE
(29) Perchellet, J; Cancer Res 1987, V47, P6302 CAPLUS
(30) Rapp, L; Biochim Biophys Acta 1998, V1378, P1
(31) Reisinger, E; Lancet 1990, V335, P679 MEDLINE
(32) Rice, W; J Med Chem 1996, V39, P3606 CAPLUS
(33) Rice, W; Science 1995, V270, P1194 CAPLUS
(34) Ronco, L; Genes Dev 1998, V12, P2061 CAPLUS
(35) Rose, P; N Engl J Med 1999, V340, P1144 CAPLUS
(36) Rothenberg, M; J Natl Cancer Inst 1988, V80, P1488 MEDLINE
(37) Scheffner, M; Proc Natl Acad Sci 1994, V91, P8797 CAPLUS
(38) Siegers, C; Arch Toxicol 1978, V41, P79 CAPLUS
(39) Song, S; J Virol 1999, V73, P5887 CAPLUS
(40) Stoler, M; Hum Pathol 1992, V23, P117 MEDLINE
(41) Tan, T; Cancer Res 1995, V55, P4599 CAPLUS
(42) Thomas, M; Oncogene 1998, V17, P2943 CAPLUS
(43) Tong, X; Proc Natl Acad Sci 1997, V94, P4412 CAPLUS
(44) Tummino, P; Proc Natl Acad Sci 1996, V93, P969 CAPLUS
(45) Ullman, C; Biochem J 1996, V319, P229 CAPLUS
(46) von Knebel, D; Int J Cancer 1992, V51, P831
(47) White, A; Genes Dev 1994, V8, P666 CAPLUS
(48) Zimmermann, H; J Virol 1999, V73, P6209 CAPLUS
(49) zur Hausen, H; Annu Rev Microbiol 1994, V48, P427 MEDLINE

L8 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2003 ACS

AB R1R2NZSSnZNR3R4 (I) [R1-R4 = H, alkyl, acyl, aryl, etc.; R1R2,R3R4 = (CH2)lUm(CH2)p; U = bond, O, S, NH, CH2; Z = bond or where n = 1 Z may = CS; l,p = 0-6; m = 0 or 1; l+m+p.gtoreq.2; n = 1-5], inhibitors of proteins encoded by an **MPV** gene by disruption of a chelated metal cation domain, were prepd. Thus, e.g., R1R2NSSNR3R4 (R1R2,R3R4 = CH2CH2NRCH2CH2, R = 2-pyridinyl) was prepd. Data for biol. activity of I were given.

ACCESSION NUMBER: 2000:175791 CAPLUS
DOCUMENT NUMBER: 132:222549
TITLE: Preparation of bis(piperazinyl) disulfides and analogs for treatment of **papillomavirus**-mediated disorders
INVENTOR(S): Bernard, Hans-Ulrich; Tan, Yee Joo; Beerheide, Walter; Ting, Anthony Eugene; Sim, Mui Mui
PATENT ASSIGNEE(S): Institute of Molecular & Cell Biology, Singapore; Hughes, E. John L.
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000014063	A1	20000316	WO 1999-AU724	19990903

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY,

KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2342858	AA	20000316	CA 1999-2342858	19990903
AU 9958401	A1	20000327	AU 1999-58401	19990903
EP 1112250	A1	20010704	EP 1999-945758	19990903
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002524442	T2	20020806	JP 2000-568822	19990903

PRIORITY APPLN. INFO.:
AU 1998-5733 A 19980904
AU 1999-1645 A 19990715
WO 1999-AU724 W 19990903

OTHER SOURCE(S): MARPAT 132:222549

RE

(1) Anon
(2) Anon; Chromatographia 1989, 3-4, P113 CAPLUS
(3) Anon; Rubber Chem Technol 1984, 4, P744 CAPLUS
(4) Bridgestone Corporation; EP 562750 1993 CAPLUS
(5) Chertova, E; Techniques in Protein Chemistry VIII [Symp Protein Soc], 10th 1997, P231 CAPLUS
(6) Hathout, Y; Drug Metabolism and Disposition:The Biological Fate of Chemicals 1996, V24(12), P1395 CAPLUS
(7) Katritzky, A; Synlett 1990, P473 CAPLUS
(8) Kawaguchi Kagaku Kogyo Kk; JP 04208223 1992 CAPLUS
(9) Kinki Daigaku Gh; JP 07233057 A 1995 CAPLUS
(10) Kuraray Kk; JP 03063258 A 1991 CAPLUS
(11) Lycke, E; Brain Research 1972, V44(2), P603 MEDLINE
(12) McDonnell, N; Journal of Medicinal Chemistry 1997, V40(13), P1969 CAPLUS
(13) Nihon Parkerizing; JP 02304346 A 1990 CAPLUS
(14) Nippon Oil Seal Ind; JP 03178148 A 1988
(15) Ott, D; Virology 1998, V243, P287
(16) Rein, A; Journal of Virology 1990, V70(8), P4966
(17) Rice, W; Journal of Medicinal Chemistry 1996, V39(19), P3606 CAPLUS
(18) Rotstein, J; Carcinogenesis 1988, V9(9), P1547 CAPLUS
(19) The Government Of The United States Of America; WO 9609406 1996 CAPLUS
(20) Toyo Soda Mfg Kk; JP 1207376 A 1986

L8 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2003 ACS

AB The principal agent in the etiol. of **cervical cancer**, i.e., human **papillomavirus** (**HPV**) type 16, encodes three oncoproteins, E5, E6, and E7. Structural and mutational studies have identified two potential zinc-finger domains as crit. for E6 protein function. We investigated several assays to identify and characterize compds. that interfere with the binding of zinc to E6. Thirty-six compds. were selected on the basis of their structure, which would facilitate their participation in sulfhydryl residue-specific redox reactions, and were tested for their ability to release zinc from E6 protein. The zinc-ejecting compds. were then tested for their ability to inhibit E6 binding to E6-assocd. protein (E6AP) and E6-binding protein (E6BP), two coactivators of E6-mediated cellular transformation. The binding of E6 to E6BP and E6AP was measured by use of surface plasmon resonance (a technique that monitors mol. interactions by measuring changes in refractive index) and by use of in vitro translation assays. The compds. were also tested for their effects on the viability of **HPV** -contg. cell lines. Nine of the 36 tested compds. ejected zinc from E6. Two of the nine compds. inhibited the interaction of E6 with E6AP and E6BP, and one of these two, 4,4'-dithiodimorpholine, selectively inhibited cell viability and induced higher levels of p53 protein (assocd. with the induction of apoptosis [programmed cell death]) in tumorigenic **HPV** -contg. cells. We have described assay systems to identify compds., such as 4,4'-dithiodimorpholine, that can potentially interfere with the biol.

and pathol. of **HPV**. These assay systems may be useful in the development of drugs against **cervical cancer**, genital **warts**, and asymptomatic infections by genital **HPVs**.

ACCESSION NUMBER: 1999:507293 CAPLUS
DOCUMENT NUMBER: 132:87659
TITLE: Potential drugs against **cervical cancer**: zinc-ejecting inhibitors of the human **papillomavirus** type 16 E6 oncoprotein
AUTHOR(S): Beerheide, Walter; Bernard, Hans-Ulrich; Tan, Yee-Joo; Ganesan, Arasu; Rice, William G.; Ting, Anthony E.
CORPORATE SOURCE: Screening for Novel Inhibitors Laboratory, Institute of Molecular and Cell Biology, Singapore, 117609, Singapore
SOURCE: Journal of the National Cancer Institute (1999), 91(14), 1211-1220
CODEN: JNCIEQ; ISSN: 0027-8874
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

RE
(1) Androphy, E; EMBO J 1987, V6, P989 CAPLUS
(2) Bartsch, D; EMBO J 1992, V11, P2283 CAPLUS
(3) Bosch, F; J Virol 1990, V64, P4743 CAPLUS
(4) Chan, S; J Virol 1995, V69, P3074 CAPLUS
(5) Chen, J; J Biol Chem 1998, V273, P13537 CAPLUS
(6) Chen, J; Science 1995, V269, P529 CAPLUS
(7) Crook, T; Cell 1991, V67, P547 CAPLUS
(8) Dalal, S; J Virol 1996, V70, P683 CAPLUS
(9) Daniels, P; FEBS Lett 1997, V416, P6 CAPLUS
(10) Desaintes, C; EMBO J 1997, V16, P504 CAPLUS
(11) Dsouza, M; Trends Genet 1997, V13, P497 CAPLUS
(12) Etscheid, B; Virology 1994, V205, P583 CAPLUS
(13) Frederickson, C; J Neurosci Methods 1987, V20, P91 CAPLUS
(14) Grossman, S; Oncogene 1989, V4, P1089 CAPLUS
(15) Hawley-Nelson, P; EMBO J 1989, V8, P3905 CAPLUS
(16) Howley, P; Field's virology 1996, P2045
(17) Huibregtse, J; Mol Cell Biol 1993, V13, P775 CAPLUS
(18) International Agency for Research on Cancer; Human papillomaviruses 1995, V64
(19) Kanda, T; Virology 1991, V185, P536 CAPLUS
(20) Kearns, P; Drug Discov Today 1998, V3, P113 CAPLUS
(21) Klingelhutz, A; Nature 1996, V380, P79 CAPLUS
(22) Klug, A; FASEB J 1995, V9, P597 CAPLUS
(23) Lamberti, C; EMBO J 1990, V9, P1907 CAPLUS
(24) Lehman, T; Carcinogenesis 1993, V14, P1491 CAPLUS
(25) Lehman, T; Carcinogenesis 1993, V14, P833 CAPLUS
(26) Mackay, J; Trends Biochem Sci 1998, V23, P1 CAPLUS
(27) Malmqvist, M; Curr Opin Immunol 1993, V5, P282 CAPLUS
(28) Meyers, G; Human papillomaviruses 1994, PII-E6
(29) Meyers, G; Human papillomaviruses 1995, P47
(30) Nakagawa, S; Virology 1995, V212, P535 CAPLUS
(31) Polyak, K; Nature 1997, V389, P300 CAPLUS
(32) Rice, W; J Med Chem 1996, V39, P3606 CAPLUS
(33) Rice, W; Nat Med 1997, V3, P341 CAPLUS
(34) Rice, W; Nature 1993, V361, P473 CAPLUS
(35) Rice, W; Proc Natl Acad Sci 1992, V89, P7703 CAPLUS
(36) Rice, W; Science 1995, V270, P1194 CAPLUS
(37) Scheffner, M; Proc Natl Acad Sci 1994, V91, P8797 CAPLUS
(38) Sedman, S; J Virol 1991, V65, P4860 CAPLUS
(39) Sherman, L; Virology 1997, V237, P296 CAPLUS
(40) Stanley, M; Papillomavirus Rep 1994, V5, P141
(41) Steele, C; Cancer Res 1992, V52, P4706 CAPLUS

(42) Tan, T; Cancer Res 1995, V55, P4599 CAPLUS
(43) Tew, K; Cancer Res 1994, V54, P4313 CAPLUS
(44) Tong, X; Proc Natl Acad Sci 1997, V94, P4412 CAPLUS
(45) Tummino, P; Proc Natl Acad Sci 1996, V93, P969 CAPLUS
(46) Ullman, C; Biochem J 1996, V319, P229 CAPLUS
(47) Vandevelde, M; AIDS Res Hum Retroviruses 1996, V12, P567 CAPLUS
(48) von Knebel Doeberitz, M; Int J Cancer 1992, V51, P831 MEDLINE
(49) Vousden, K; J Virol 1989, V63, P2340 CAPLUS
(50) White, A; Genes Dev 1994, V8, P666 CAPLUS
(51) Wright, T; Papillomavirus Rep 1994, V5, P175
(52) Yu, X; Chem Res Toxicol 1995, V8, P586 CAPLUS
(53) zur Hausen, H; Annu Rev Microbiol 1994, V48, P427 MEDLINE

9 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
AN **1990:92775** CAPLUS
DN 112:92775
TI The E6 and E7 genes of HPV-18 are sufficient for inducing two-stage in vitro transformation of human keratinocytes
AU Barbosa, Miguel S.; Schlegel, Richard
CS Lab. Cell. Oncol., Natl. Cancer Inst., Bethesda, MD, 20892, USA
SO Oncogene (1989), 4(12), 1529-32
CODEN: ONCNES; ISSN: 0950-9232
DT Journal
LA English
AB Using a recently described keratinocyte assay, HPV-18 DNA was shown to induce 2 progressive steps in cellular transformation (a large cell and a small cell stage). Both steps of this keratinocyte transformation can be achieved with a subgenomic fragment contg. only the HPV-18 regulatory region and E6/E7 genes. Similar to cell lines transformed by the complete HPV-18 genome, keratinocytes transformed by the HPV-18 E6/E7 genes express the major early viral protein (E7) but are non-tumorigenic in nude mice. Interestingly, HPV-18 DNA was noted to be 5 times more efficient than HPV-16 DNA for in vitro keratinocyte transformation, regardless of the method of DNA transfection.

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L10 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
AN **1999:507293** CAPLUS
DN 132:87659
TI Potential drugs against cervical cancer: zinc-ejecting inhibitors of the human papillomavirus type 16 E6 oncoprotein
AU Beerheide, Walter; Bernard, Hans-Ulrich; Tan, Yee-Joo; Ganesan, Arasu; Rice, William G.; Ting, Anthony E.
CS Screening for Novel Inhibitors Laboratory, Institute of Molecular and Cell Biology, Singapore, 117609, Singapore
SO Journal of the National Cancer Institute (1999), 91(14), 1211-1220
CODEN: JNCIEQ; ISSN: 0027-8874
PB Oxford University Press
DT Journal
LA English
AB The principal agent in the etiol. of cervical cancer, i.e., human papillomavirus (HPV) type 16, encodes three oncoproteins, E5, E6, and E7. Structural and mutational studies have identified two potential zinc-finger domains as crit. for E6 protein function. We investigated several assays to identify and characterize compds. that interfere with the binding of zinc to E6. Thirty-six compds. were selected on the basis of their structure, which would facilitate their participation in sulfhydryl residue-specific redox reactions, and were tested for their ability to release zinc from E6 protein. The zinc-ejecting compds. were then tested for their ability to inhibit E6 binding to E6-assocd. protein (E6AP) and E6-binding protein (E6BP), two coactivators of E6-mediated cellular transformation. The binding of E6 to E6BP and E6AP was measured by use of surface plasmon resonance (a technique that monitors mol. interactions by measuring changes in refractive index) and by use of in vitro translation assays. The compds. were also tested for their effects on the viability of HPV-contg. cell lines. Nine of the 36 tested compds. ejected zinc from E6. Two of the nine compds. inhibited the interaction of E6 with E6AP and E6BP, and one of these two, 4,4'-dithiodimorpholine, selectively inhibited cell viability and induced higher levels of p53 protein (assocd. with the induction of apoptosis [programmed cell death]) in tumorigenic HPV-contg. cells. We have described assay systems to identify compds., such as 4,4'-dithiodimorpholine, that can potentially interfere with the biol. and pathol. of HPV. These assay systems may be useful in the development of drugs against cervical cancer, genital warts, and asymptomatic infections by genital HPVs.
RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
AN **1980:69670** CAPLUS
DN 92:69670
TI Inhibition of cis-platinum nephrotoxicity by diethyldithiocarbamate rescue in a rat model
AU Borch, Richard F.; Pleasants, Michael E.
CS Dep. Chem., Univ. Minnesota, Minneapolis, MN, 55455, USA
SO Proceedings of the National Academy of Sciences of the United States of America (1979), 76(12), 6611-14
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
AB The nephrotoxic effects of cis-dichlorodiammineplatinum(II) (NSC-119875) [15663-27-1] administered to male F344 rats at the median LD (LD50; 7.5 mg/kg) were inhibited by treatment with Na diethyldithiocarbamate [148-18-5] (500 or 750 mg/kg) between 1 and 4 h after cis-platinum administration. Those animals receiving cis-platinum alone had mean serum blood urea N levels of 234 mg/dl at the time of maximal toxicity. When dithiocarbamate rescue was carried out after cis-platinum treatment, mean blood urea N levels were 56-95 mg/dl; kidney sections were grossly normal with a barely discernible band of degeneration at the corticomedullary junction. Gastrointestinal toxicity was obsd. in >95% of the cis-platinum-treated rats but was totally absent in those receiving subsequent rescue treatment. A significant decrease in wt. loss was also obsd. in the dithiocarbamate-rescued rats. Based on the chem. of platinum-sulfur interactions and the obsd. time-dependence of the rescue treatment, it is suggested that dithiocarbamate exerts its effects via competitive chelation and removal of Pt coordinated to protein-bound SH groups of the kidney tubule cells.

AN **1995:434468** CAPLUS
DN 122:210936
TI Functional p53 protein in human papillomavirus-positive cancer cells
AU Butz, Karin; Shahabeddin, Lili; Geisen, Caroline; Spitkovsky, Dimitry; Ullmann, Angela; Hoppe-Seyler, Felix
CS Projektgruppe Angewandte Tumorvirologie, Deutsches Krebsforschungszentrum, Heidelberg, D-69120, Germany
SO Oncogene (1995), 10(5), 927-36
CODEN: ONCNES; ISSN: 0950-9232
PB Stockton
DT Journal
LA English
AB There is accumulating evidence that the p53 protein contributes to tumor suppression by stimulating the transcription of specific cellular genes, such as the cell cycle control gene WAF1/ClP1. P53-mediated transcriptional activation is inhibited in cotransfection assays by overexpressed E6 protein from cancer-assocd. human papillomavirus (HPV) types, pointing at a possible mol. mechanism by which these viruses contribute to malignant cell transformation. Here we analyzed the transcriptional transactivation function of endogenous p53 protein in a series of cervical cancer cell lines, which express the E6 gene from integrated viral sequences. Transient and stable transfection analyses employing p53-responsive reporter constructs indicated that HPV-pos. cervical cancer cells contained transactivating p53 protein. Treatment of HPV-pos. cells with genotoxic agents, such as mitomycin C, cisplatin, or u.v. irradn., resulted in an increase of nuclear p53 protein levels and enhanced binding of p53 to a p53-recognition site. These effects were accompanied by an increase of WAF1/ClP1 mRNA levels. In several HPV-pos. cell lines, these mol. events were linked to a cell cycle arrest in G1. In contrast, cancer cells contg. mutant p53 genes did not contain transactivating endogenous p53 protein and lacked the p53-mediated response to DNA damaging agents. These results indicate that the tumorigenic phenotype of HPV-pos. cancer cell lines does not necessarily correlate with a lack of basal or DNA damage induced p53 activities and that therefore the presence of high risk HPV sequences is not functionally equiv. to the loss of p53 function through somatic mutations of the p53 gene.

AN **1995:502169** CAPLUS
DN 123:76166
TI Analysis of genomic sequences of 95 papillomavirus types: uniting typing, phylogeny, and taxonomy
AU Chan, Shih-Yen; Delius, Hajo; Halpern, Aaron L.; Bernard, Hans-Ulrich
CS Institute of Molecular and Cell Biology, National University of Singapore, Singapore, 0511, Singapore
SO Journal of Virology (1995), 69(5), 3074-83
CODEN: JOVIAM; ISSN: 0022-538X
PB American Society for Microbiology
DT Journal
LA English
AB Our aim was to study the phylogenetic relationships of all known papillomaviruses (PVs) and the possibility of establishing a supratype taxonomic classification based on this information. Of the many detectably homologous segments present in PV genomes, a 291-bp segment of the L1 gene is notable because it is flanked by the MY09 and MY11 consensus primers and contains highly conserved amino acid residues which simplify sequence alignment. We detd. the MY09-MY11 sequences of human PV type 20 (HPV-20), HPV-21, HPV-22, HPV-23, HPV-24, HPV-36, HPV-37, HPV-38, HPV-48, HPV-50, HPV-60, HPV-70, HPV-72, HPV-73, ovine (sheep) PV, bovine PV type 3 (BPV-3), BPV-5, and BPV-6 and created a database which now encompasses HPV-1 to HPV-70, HPV-72, HPV-73, seven yet untyped HPV genomes, and 15 animal PV types. Three addnl. animal PVs were analyzed on the basis of other sequence data. We constructed phylogenies based on partial L1 and E6 gene sequences and distinguished five major clades that call supergroups. One of them unites 54 genital PV types, which can be further divided into eleven groups. The second supergroup has 24 types and unites most PVs that are typically found in epidermodysplasia verruciformis patients but also includes several types typical of other cutaneous lesions, like HPV-4. The third supergroup units the six known ungulate fibropapillomaviruses, the fourth includes the cutaneous ungulate PVs BPV-3, BPV-4, and BPV-6, and the fifth includes HPV-1, HPV-41, HPV-63, the canine oral PV, and the cottontail rabbit PV. The chaffinch PV and two rodent PVs, Micromys minutus PV and Mastomys natalensis PV, are left ungrouped because of the relative isolation of each of their lineages. Within most supergroups, groups formed on the basis of cladistic principles unite phenotypically similar PV types. We discuss the basis of our classification, the concept of the PV type, speciation, PV-ho

AN **1995:502169** CAPLUS
DN 123:76166
TI Analysis of genomic sequences of 95 papillomavirus types: uniting typing, phylogeny, and taxonomy
AU Chan, Shih-Yen; Delius, Hajo; Halpern, Aaron L.; Bernard, Hans-Ulrich
CS Institute of Molecular and Cell Biology, National University of Singapore, Singapore, 0511, Singapore
SO Journal of Virology (1995), 69(5), 3074-83
CODEN: JOVIAM; ISSN: 0022-538X
PB American Society for Microbiology
DT Journal
LA English
AB Our aim was to study the phylogenetic relationships of all known papillomaviruses (PVs) and the possibility of establishing a supratype taxonomic classification based on this information. Of the many detectably homologous segments present in PV genomes, a 291-bp segment of the L1 gene is notable because it is flanked by the MY09 and MY11 consensus primers and contains highly conserved amino acid residues which simplify sequence alignment. We detd. the MY09-MY11 sequences of human PV type 20 (HPV-20), HPV-21, HPV-22, HPV-23, HPV-24, HPV-36, HPV-37, HPV-38, HPV-48, HPV-50, HPV-60, HPV-70, HPV-72, HPV-73, ovine (sheep) PV, bovine PV type 3 (BPV-3), BPV-5, and BPV-6 and created a database which now encompasses HPV-1 to HPV-70, HPV-72, HPV-73, seven yet untyped HPV genomes, and 15 animal PV types. Three addnl. animal PVs were analyzed on the basis of other sequence data. We constructed phylogenies based on partial L1 and E6 gene sequences and distinguished five major clades that call supergroups. One of them unites 54 genital PV types, which can be further divided into eleven groups. The second supergroup has 24 types and unites most PVs that are typically found in epidermodysplasia verruciformis patients but also includes several types typical of other cutaneous lesions, like HPV-4. The third supergroup units the six known ungulate fibropapillomaviruses, the fourth includes the cutaneous ungulate PVs BPV-3, BPV-4, and BPV-6, and the fifth includes HPV-1, HPV-41, HPV-63, the canine oral PV, and the cottontail rabbit PV. The chaffinch PV and two rodent PVs, Micromys minutus PV and Mastomys natalensis PV, are left ungrouped because of the relative isolation of each of their lineages. Within most supergroups, groups formed on the basis of cladistic principles unite phenotypically similar PV types. We discuss the basis of our classification, the concept of the PV type, speciation, PV-host evolution, and ests. of their rates of evolution.

AN **1995:719736** CAPLUS
DN 123:195281
TI Interaction of papillomavirus E6 oncoproteins with a putative calcium-binding protein
AU Chen, Jason J.; Reid, Carl E.; Band, Vimla; Androphy, Elliot J.
CS Sch. Med., Tufts Univ., Boston, MA, 02111, USA
SO Science (Washington, D. C.) (1995), 269(5223), 529-31
CODEN: SCIEAS; ISSN: 0036-8075
PB American Association for the Advancement of Science
DT Journal
LA English
AB Human papillomaviruses (HPVs) are assocd. with the majority of cervical cancers and encode a transforming protein, E6, that interacts with the tumor suppressor protein p53. Because E6 has p53-independent transforming activity, the yeast two-hybrid system was used to search for other E6-binding proteins. One such protein, E6BP, interacted with cancer-assocd. HPV E6 and with bovine papillomavirus type 1 (BPV-1) E6. The transforming activity of BPV-1 E6 mutants correlated with their E6BP-binding ability. E6BP is identical to a putative calcium-binding protein, ERC-55, that appears to be localized in the endoplasmic reticulum.

AN **1992:609888** CAPLUS
DN 117:209888
TI Degradation of p53 can be targeted by HPV E6 sequences distinct from those required for p53 binding and trans-activation
AU Crook, Tim; Tidy, John A.; Vousden, Karen H.
CS Med. Sch., St. Mary's Hosp., London, W2 1PG, UK
SO Cell (Cambridge, MA, United States) (1991), 67(3), 547-56
CODEN: CELLB5; ISSN: 0092-8674
DT Journal
LA English
AB Human papillomavirus (HPV) types 16 and 18 appear to play a role in the development of ano-genital malignancies, whereas HPV 6 and 11 are usually assocd. with benign lesions. One HPV 16 oncoprotein, E6, complexes with and promotes degrdn. of the cellular tumor suppressor p53. Here the authors show that E6 proteins of both oncogenic and benign HPV types assoc. in vitro with p53, but binding by E6 proteins of benign HPV types cannot target p53 for degrdn. A C-terminal region of E6 conserved among all HPV types is important for p53 binding. However, N-terminal sequences of E6 conserved only between oncogenic HPV types are necessary to direct p53 degrdn. P53 binding by E6 appears necessary but not sufficient for this activity. All E6 proteins tested showed comparable transcriptional trans-activating activity, a property that does not require the ability to bind or direct degrdn. of p53.

AN **1989:171017** CAPLUS
DN 110:171017
TI The human papilloma virus-16 E7 oncoprotein is able to bind to the retinoblastoma gene product
AU Dyson, Nicholas; Howley, Peter M.; Muenger, Karl; Harlow, Ed
CS Cold Spring Harbor Lab., Spring Harbor, NY, 11724, USA
SO Science (Washington, DC, United States) (1989), 243(4893), 934-7
CODEN: SCIEAS; ISSN: 0036-8075
DT Journal
LA English
AB Deletions or mutations of the retinoblastoma gene, RB1, are common features of many tumors and tumor cell lines. Recently, the RB1 gene product, p105-RB, has been shown to form stable protein/protein complexes with oncoproteins of 2 DNA tumor viruses, the adenovirus E1A proteins and the simian virus 40 (SV40) large T antigen. Neither of these viruses is thought to be assocd. with human cancer, but they can cause tumors in rodents. Binding between the RB anti-oncoprotein and the adenovirus or SV40 oncoprotein can be recapitulated in vitro with coimmunopptn. mixing assays. These assays have been used to demonstrate that the E7 oncoprotein of the human papilloma virus type 16 can form similar complexes with p105-RB. Human papilloma virus 16 is found assocd. with approx. 50 percent of cervical carcinomas. These 3 DNA viruses may utilized similar mechanisms in transformation. The results implicate RB binding as a possible step in human papilloma virus-assocd. carcinogenesis.

L17 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
AN **1995:244480** CAPLUS
DN 122:95783
TI Comparative studies on the pharmacokinetics of hydrophilic prolinedithiocarbamate, sarcosinedithiocarbamate and the less hydrophilic diethyldithiocarbamate
AU Frank, N.; Christmann, A.; Frei, E.
CS German Cancer Research Center, Division of Molecular Toxicology, Im Neuenheimer Feld 280, Heidelberg, 69120, Germany
SO Toxicology (1995), 95(1-3), 113-22
CODEN: TXCYAC; ISSN: 0300-483X
PB Elsevier
DT Journal
LA English
AB The pharmacokinetics of the antitoxic and anticarcinogenic compds. diethyldithiocarbamate, prolinedithiocarbamate and sarcosinedithiocarbamate were compared in rats. The bioavailability, the distribution in the organism, the oxidn. to thiuramdisulfides, the cleavage to CS2 and the excretion in urine and bile were investigated. The results showed different behavior of the three compds. The more toxic diethyldithiocarbamate had a short in vivo half- life, was oxidized to tetraethylthiuramdisulfide in blood, and was metabolized to high yields of CS2 in 24 h. In contrast, prolinedithiocarbamate was more stable in vivo, was found predominantly in the urinary tract and was excreted in urine. The differences could not be explained by the presence of the carboxy group in the latter dithiocarbamate, since sarcosinedithiocarbamate, which also contains a carboxy group, behaved like diethyldithiocarbamate.

AN **1993:139404** CAPLUS
DN 118:139404
TI Induction of nuclear accumulation of the tumor-suppressor protein p53 by DNA-damaging agents
AU Fritsche, Michael; Haessler, Christel; Brandner, Gerhard
CS Inst. Med. Mikrobiol. Hyg., Univ. Freiburg, Freiburg, Germany
SO Oncogene (1993), 8(2), 307-18
CODEN: ONCNES; ISSN: 0950-9232
DT Journal
LA English
AB Cancer therapy drugs, such as cisplatin, mitomycin C, etoposide and other compds., and energy-rich radiation act on cellular DNA. These agents induce nuclear accumulation of the tumor-suppressor protein p53 in fibroblastoid cells, as well as in epithelioid normal and immortalized cells of murine, simian, and human origin. The p53 accumulation starts a few hours after treatment and is detectable in surviving cells for at least 20 days. The accumulation occurs because of increased p53 protein stability and depends on ongoing translocation. It is not the result of enhanced gene expression. A no. of cell cycle inhibitors do not affect the p53 protein accumulation, suggesting that the process may start from several points in the cell cycle. Since the increase in the nuclear p53 protein levels occurs within a few hours in most normal diploid cells, it is unlikely that the accumulated p53 protein is derived from a mutated p53 gene. The DNA damage-induced p53 accumulation may either inhibit cell growth, allowing DNA repair processes, or in the case of severe damage it can initiate apoptosis.

AN **1998:460697** CAPLUS
DN 129:173955
TI Basal and human papillomavirus E6 oncoprotein-induced degradation of Myc proteins by the ubiquitin pathway
AU Gross-Mesilaty, Shlomit; Reinstein, Eyal; Bercovich, Beatrice; Tobias, Karin E.; Schwartz, Alan L.; Kahana, Chaim; Ciechanover, Aaron
CS Department of Biochemistry and the Rappaport Family Institute for Research in the Medical Sciences, The Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, 31096, Israel
SO Proceedings of the National Academy of Sciences of the United States of America (1998), 95(14), 8058-8063
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB We have previously shown that the degrdn. of c-myc and N-myc in vitro is mediated by the ubiquitin system. However, the role of the system in targeting the myc proteins in vivo and the identity of the conjugating enzymes and possible ancillary proteins involved has remained obscure. Here we report that the degrdn. of the myc proteins in cells is inhibited by lactacystin and MG132, two inhibitors of the 20S proteasome. Inhibition is accompanied by accumulation of myc-ubiquitin conjugates. Dissection of the ancillary proteins involved revealed that the high-risk human papillomavirus oncoprotein E6-16 stimulates conjugation and subsequent degrdn. of the myc proteins in vitro. Expression of E6-16 in cells results in significant shortening of the t1/2 of the myc proteins with subsequent decrease in their cellular level. Anal. of the conjugating enzymes revealed that under basal conditions the proteins can be conjugated by two pairs of E2s and E3s-E2-14 kDa and E3.alpha. involved in the "N-end rule" pathway, and E2-F1 (UbcH7) and E3-Fos involved also in conjugation of c-Fos. In the presence of E6-16, a third pair, E2-F1 and E6-AP mediate conjugation of myc by means of a mechanism that appears to be similar to that involved in the targeting of p53, formation of a myc E6.E6-AP targeting complex. It is possible that in certain cells E6-mediated targeting of myc prevents myc-induced apoptosis and thus ensures maintenance of viral infection.
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AN **1993:142054** CAPLUS
DN 118:142054
TI Cloning and expression of the cDNA for E6-AP, a protein that mediates the interaction of the human papillomavirus E6 oncoprotein with p53
AU Huibregtse, Jon M.; Scheffner, Martin; Howley, Peter M.
CS Lab. Tumor Virus Biol., Natl. Cancer Inst., Bethesda, MD, 20892, USA
SO Molecular and Cellular Biology (1993), 13(2), 775-84
CODEN: MCEBD4; ISSN: 0270-7306
DT Journal
LA English
AB The E6 oncoproteins of the cancer-assocd. or high-risk human papillomaviruses (HPVs) target the cellular p53 protein. The assocn. of E6 with p53 leads to the specific ubiquitination and degrdn. of p53 in vitro, suggesting a model by which E6 deregulates cell growth control by the elimination of the p53 tumor suppressor protein. Complex formation between E6 and p53 requires an addnl. cellular factor, designated E6-AP (E6-assocd. protein), which has a native and subunit mol. mass of approx. 100 kDa. Here the purifn. of E6-AP and the cloning of its corresponding cDNA, which contains a novel open reading frame encoding 865 amino acids is reported. E6-AP, translated in vitro, has the following properties: (i) it assocs. with wild-type p53 in the presence of the HPV16 E6 protein and simultaneously stimulates the assocn. of E6 with p53, (ii) it assocs. with the high-risk HPV16 and HPV18 E6 proteins in the absence of p53, and (iii) induces the E6- and ubiquitin-dependent degrdn. of p53 in vitro.

L21 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
AN **1999:33268** CAPLUS
DN 130:208175
TI Inhibition of Bak-induced apoptosis by HPV-18 E6
AU Thomas, Miranda; Banks, Lawrence
CS International Centre for Genetic Engineering and Biotechnology, Trieste, I-34012, Italy
SO Oncogene (1998), 17(23), 2943-2954
CODEN: ONCNES; ISSN: 0950-9232
PB Stockton Press
DT Journal
LA English
AB Human papillomavirus (HPV) E6 proteins inhibit apoptosis in both p53-dependent and p53-independent manners. A key point in apoptosis is the regulation provided by the Bcl-2 family; and in differentiating keratinocytes, in which HPV replicates, the Bak protein is highly expressed. The authors show that HPV-18 E6 will inhibit Bak-induced apoptosis and this is mediated by an interaction between the E6 and Bak proteins resulting in degrdn. of the Bak protein in vivo. The authors also show that Bak protein interacts with the ubiquitin ligase, E6AP, and that a mutant of Bak defective in E6AP binding is overexpressed in comparison with wild type. These studies suggest that Bak is probably the first naturally occurring target of E6AP to be identified.
RE.CNT 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

N °**1999:398754** CAPLUS
DN 131:168536
TI The human papillomavirus type 16 E6 gene alone is sufficient to induce carcinomas in transgenic animals
AU Song, Shiyu; Pitot, Henry C.; Lambert, Paul F.
CS McArdle Laboratory for Cancer Research, University of Wisconsin Medical School, Madison, WI, 53706, USA
SO Journal of Virology (1999), 73(7), 5887-5893
CODEN: JOVIAM; ISSN: 0022-538X
PB American Society for Microbiology
DT Journal
LA English
AB High-risk human papillomaviruses (HPVs) are the causative agents of certain human cancers. HPV type 16 (HPV16) is the papillomavirus most frequently assocd. with cervical cancer in women. The E6 and E7 genes of HPV are expressed in cells derived from these cancers and can transform cells in tissue culture. Animal expts. have demonstrated that E6 and E7 together cause tumors. The authors showed previously that E6 and E7 together or E7 alone could induce skin tumors in mice when these genes were expressed in the basal epithelia of the skin. In this study, the authors investigated the role that the E6 gene plays in carcinogenesis. The authors generated K14E6 transgenic mice, in which the HPV16 E6 gene was directed in its expression by the human keratin 14 promoter (hK14) to the basal layer of the epidermis. The authors found that E6 induced cellular hyperproliferation and epidermal hyperplasia and caused skin tumors in adult mice. Interestingly, the tumors derived from E6 were mostly malignant, as opposed to the tumors from E7 mice, which were mostly benign. This result leads the authors' to hypothesize that E6 may contribute differently than E7 to HPV-assocd. carcinogenesis; whereas E7 primarily contributes to the early stages of carcinogenesis that lead to the formation of benign tumors, E6 primarily contributes to the late stages of carcinogenesis that lead to malignancy.
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